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ROLE OF ALLERGY IN ATELECTASIS IN CHILDREN

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LOS ANGELES

Atelectasis has been defined by Van Allen and Lindskog [1] as "an airless state of the lungs with collapse of the alveoli. No reference is implied to consolidation by replacement of air with exudate, transudate or other substance."

Atelectasis, other than that which is congenital, is due to obstruction to the passage of air, with subsequent absorption of the retained air and collapse of the alveoli. The extent of the collapse of the lung depends first on the location of the obstruction in the bronchial tree and secondly on the duration of the occlusion.[2]

Massive atelectasis due to the occlusion of a main bronchus has been described as having occurred during an asthmatic attack by various observers. The first recorded case of this type was that reported by Sante,[3] in 1928. He described a case of massive collapse of the right lung which occurred during an asthmatic attack in an adult. However, this patient also had pneumothorax, a development which was thought to be most probably due to a rupture of the visceral pleura.

Wilmer, Cobe and Lee,[4] in 1930, noted a definite relation between allergy and postoperative atelectasis. A high percentage of their patients with postoperative atelectasis gave a history of or had definite allergy.

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1. Van Allen, C. M., and Lindskog, G. E.: Obstructive Pulmonary Atelectasis: Problems of Pathogenesis and Clinical Management, Arch. Surg. **21**:1195 (Dec., pt. 2) 1930.

2. Manges, W. F., and Farrell, J. T., Jr.: Am. J. Roentgenol. **30**:429, 1933.

3. Sante, L. R.: Am. J. Roentgenol. **20**:213, 1928.

4. Wilmer, H. B.; Cobe, H. M., and Lee, W. E.: Ann. Surg. **91**:651, 1930.

Tucker,[5] in 1931, was the first to describe the actual mechanism of atelectasis in asthma. This mechanism was demonstrated bronchoscopically. We quote his observations:

> A girl, 12 years of age, a patient of Drs. Wilmer and Lee, during an asthmatic attack presented atelectasis of the right lung. The lesion which was demonstrated on physical and roentgen examination . . . gave a typical picture of collapse on the right side, such as is seen in postoperative cases. At the request of Drs. Wilmer and Lee, I made a bronchoscopic examination of this patient and found the mechanism of the condition identical with that in postoperative massive collapse. A large quantity of obstructive secretion was aspirated, with a partial clearing of the lung immediately. . . . After forty-eight hours there was a gradual recurrence of the atelectasis limited to the upper and middle lobes. . . . A second bronchoscopy was done, and again a considerable quantity of obstructive secretion was removed from the bronchus of the middle lobe and of the upper lobe of the right lung. The main bronchus, however, was not completely obstructed. Following the second bronchoscopy, the lung cleared promptly . . . and after forty-eight hours was entirely clear, the asthmatic attack having subsided.

Peshkin and Fineman,[6] in 1931, and Kahn,[7] in 1932, each reported a case of nonposttraumatic and nonpostoperative massive pulmonary collapse in an asthmatic child. Miller and his associates,[8] in 1935, reported 11 cases of "allergic bronchopneumonia," which they attributed to simultaneous occurrence of atelectasis and allergic reaction in the parenchyma of the lungs. Maxwell,[9] in 1937, reported a case of massive collapse of the lung which occurred in a 13 year old asthmatic boy. On bronchoscopic examination a thick plug of mucus was found and removed, with subsequent aeration of the lung and return of the mediastinal contents to normal position within twenty-four hours.

Brunn and Brill[10] pointed out that massive collapse and various other types of atelectasis are but different stages of the same condition. Clinical and experimental evidence seems to favor the theory that bronchial obstruction is the most common single factor in the production of atelectasis. No matter what the nature of the obstruction, complete occlusion of a bronchus, owing to the absorption of the entrapped air by circulating blood, speedily results in atelectasis of the portion of the lung which that bronchus normally supplies.

The clinical symptoms of atelectasis or massive collapse as they appeared in the patients we are presenting were cough, fever and dyspnea occurring during or after an asthmatic attack. The degree of cyanosis

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5. Tucker, G.: Bronchoscopic Observations on Obstructive Pulmonary Atelectasis, Arch. Otolaryng. **13**:315 (March) 1931.

6. Peshkin, M. M., and Fineman, A. H.: Acute Massive Atelectasis and Asthma, Am. J. Dis. Child. **42**:590 (Sept.) 1931.

7. Kahn, I. S.: Texas State J. Med. **28**:416, 1932.

8. Miller, H.; Piness, G.; Finegold, B. F., and Friedman, T. B.: J. Pediat. **7**:768, 1935.

9. Maxwell, J.: St. Barth. Hosp. Rep. **70**:183, 1937.

10. Brunn, H., and Brill, S.: Ann. Surg. **92**:801, 1930.

was variable. Several of the patients had pain in the chest at the onset of the attack. The physical conditions depended entirely on the degree of involvement of the lung, but usually there were absence of normal breath sounds, dulness to flatness on percussion over the affected area and bronchophony or bronchial breathing. The most important sign from the diagnostic point of view is the shift of the heart toward the involved side.

The diagnosis of atelectasis in an asthmatic or allergic child presents the problem of ruling out the presence of pneumonia. The patient with atelectasis complicating asthma has a cold, moist skin and does not appear as ill as one with the same amount of lung tissue involved in a pneumonic process.

We wish to report the occurrence of atelectasis in 7 allergic children. In some patients the collapse involved only part of a lobe; in others, either an entire lobe or the complete lung was affected. The condition in 6 of the cases was nontraumatic and nonpostoperative.

REPORT OF CASES

CASE 1.—B. A., a boy 11 years of age, was admitted to the Children's Memorial Hospital on June 29, 1937, with a history of having been well except for intermittent attacks of asthma until a week prior to admission, when a watery nasal discharge developed. The day before admission, the boy had fever and complained of pain between the shoulder blades. This was followed by a cough that was nonproductive. These symptoms were associated with abdominal pain at the time of admission. The past history revealed that he had had asthma since the age of 7 years, the last severe attack having taken place three weeks prior to admission. He had had injections for the asthma and had obtained relief until the spring of 1937, when three severe attacks occurred. There was also a history of symptoms of hay fever, lasting from June until frost, for the past six years. There were no symptoms of allergy in any other members of the family. The past surgical history was negative except for an adenoidectomy and a tonsillectomy in 1936.

Examination revealed a well developed child with a temperature of 102.6 F., dyspnea and cough. The throat was slightly red. There was marked limitation of motion of the entire left side of the chest, with dulness and suppression, bronchial breathing and scattered fine rales over the left lung. The apex beat of the heart was palpated in the left anterior axillary line. No cardiac murmurs were heard. There was no cyanosis. The remainder of the physical examination gave negative results. The hemoglobin content of the blood was 80 per cent, and the red cell count was 4,800,000. The white cell count was 21,000, with 80 per cent neutrophils, 20 per cent lymphocytes and no eosinophils. Roentgenograms confirmed the diagnosis of complete collapse of the left lung (fig. 1 *A*).

Dr. Paul Holinger performed a bronchoscopic examination on the boy the following day and reported that the larynx was red and thickened, that the trachea and the right main bronchus contained a moderate amount of purulent secretions, that the left main bronchus was entirely occluded with thick, yellow, tenacious material and that when this was aspirated a similar secretion was coughed out of each bronchial division on the left side (fig. 1 *B*). This aspirated material was so thick and tenacious that when it was placed in a test tube the tube could be inverted

without having the secretion flow. A Giemsa stain of this material revealed that 90 per cent of the cells were eosinophils. On culture, Pneumococcus type IV and Haemophilus influenzae were found.

The patient had two more bronchoscopic examinations and made a rapid recovery, both clinically and according to roentgenographic evidence. After his discharge from the hospital, he had a moderate cough for a month (fig. 1 *C*). In February 1938 he again had an attack of coughing with fever and difficulty in breathing. No infection of the respiratory tract preceded this attack, but wheezing was present for about two days. The interval history included frequent colds with wheezing and rhinitis. Examination revealed a temperature of 102.4 F. and the

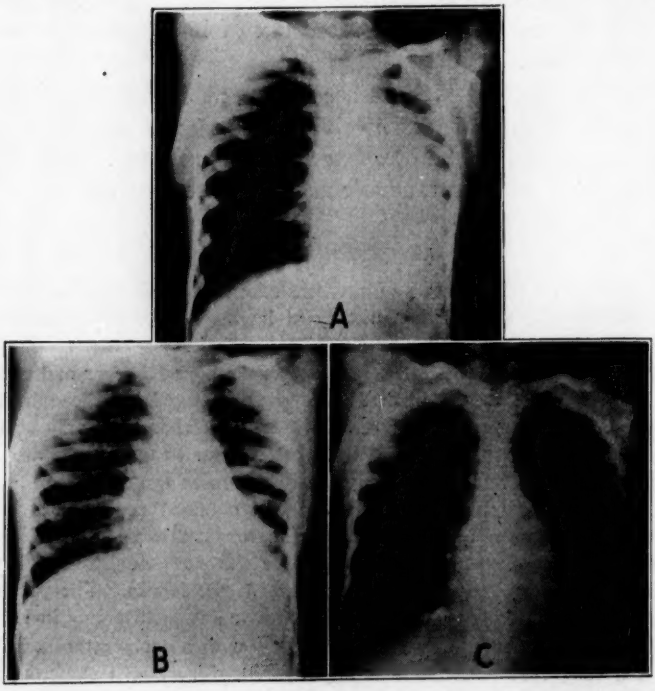

Fig. 1 (Case 1).—Roentgenograms taken: *A*, on the patient's admission to the hospital; *B*, three days after bronchoscopy; *C*, one month later.

same clinical picture as on his admission to the hospital seven months before. The left side of the chest was dull on percussion, breath sounds were absent, there was marked bronchophony and the heart was pulled far to the left. Roentgenograms again confirmed the clinical diagnosis of massive collapse of the left lung (fig. 2 *A*).

The patient was observed for seven days and again had a bronchoscopic examination. A large amount of thick white mucilage-like material was aspirated, mostly from the left main bronchus (fig. 2 *B*). Four subsequent bronchoscopies were performed, and the chest cleared up entirely (fig. 2 *C*).

Routine intradermal tests revealed positive reactions to the fall pollens, to feathers and to dog and camel hair. A recent differential count of the white blood cells revealed 11 per cent eosinophils. The boy has continued well up to the present time.

CASE 2.—M. T., a boy 7 years of age, was admitted to the Children's Memorial Hospital in October 1936 with a history of a typical, severe asthmatic attack with air hunger, cough and fever for five days. The cough was productive of a thick, whitish sputum. There was a history of a similar attack occurring six months before. The past allergic history included eczema from the age of 10 days to that of 9 months and asthma, sometimes associated with fever, from the age of 9 months. The child's birth and development were otherwise normal. The family history was unimportant except for asthma in the maternal grandfather.

On admission to the hospital the child was not acutely ill, but he had a temperature of 101.6 F. and a productive cough. The chest presented asthmatic

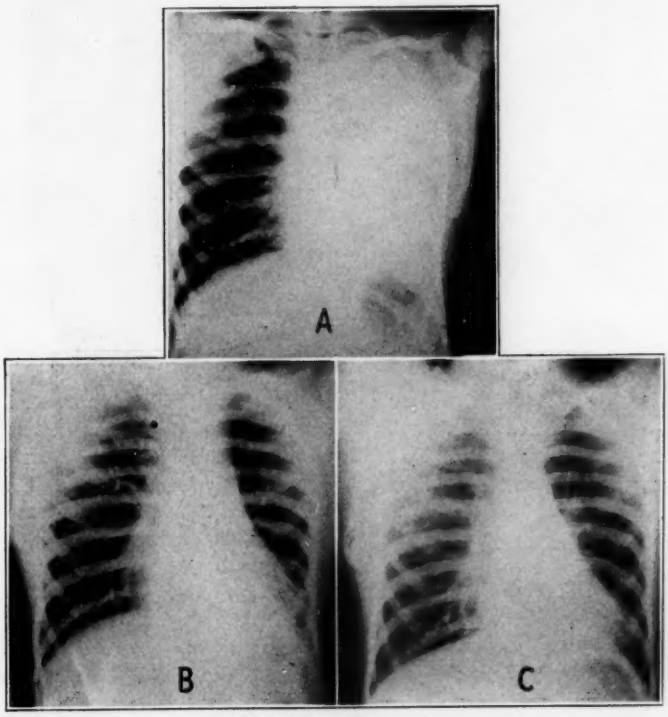

Fig. 2 (Case 1).—Roentgenograms of the same patient taken: *A*, at the time of a recurrence eight months after his first admission to the hospital; *B*, ten days later; *C*, three weeks later.

rales and wheezes. On the following day, dulness and suppression of normal breath sounds were noted over the right side of the chest anteriorly. Anteroposterior and lateral roentgenograms showed much peribronchial infiltration and atelectasis of the middle lobe of the right lung (fig. 3 *A* and *B*). The red blood cell count was 5,200,000, with 95 per cent hemoglobin; the white blood cell count was 15,900, with 56 per cent neutrophils, 34 per cent lymphocytes, 6 per cent monocytes and 4 per cent eosinophils. The tuberculin test was negative.

A bronchoscopic examination was performed by Dr. Holinger, who noted: "The laryngeal structures were inflamed and thickened. A tremendous amount

of tenacious, yellowish secretion was found in the trachea and in the right main bronchus. The orifice of the bronchus to the middle lobe was patent, but insertion of the curved aspirator into it freed a large quantity of pus."

Four subsequent bronchoscopic examinations were done, and the patient's condition improved rapidly. He was clinically and roentgenologically well in twenty-six days and was discharged from the hospital (fig. 3 *C*).

Since discharge, the child has had many asthmatic attacks, frequently followed by periods of purulent bronchitis simulating bronchiectasis. Of late he has been better, especially since offending substances have been eliminated from his diet and environment. The allergic study showed positive reactions to a number of things, including some cereals, beef, seafoods, cocoa, coffee, some nuts, orris root, kapok

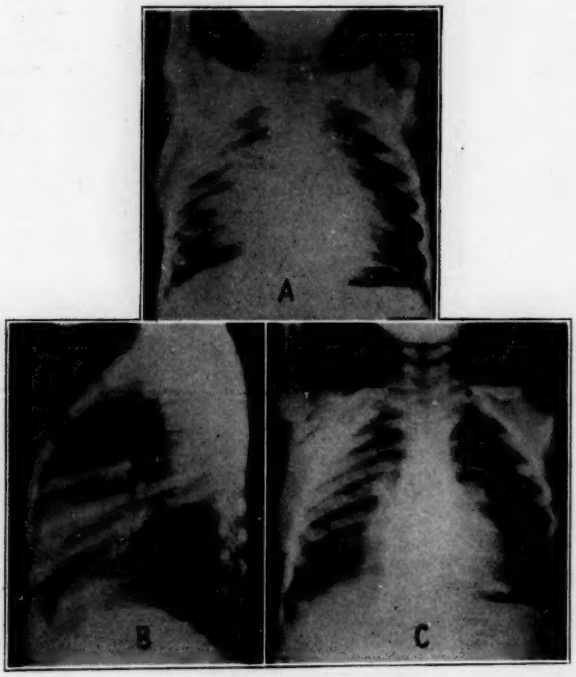

Fig. 3 (Case 2).—Roentgenograms taken during an attack. *A*, anterior view; *B*, lateral view.

and most of the animal hairs. He also had positive reactions to the fall pollens. Differential blood counts have shown an eosinophilia as high as 11 per cent.

In January 1937 there was an attack of cough with fever and purulent expectoration and the roentgen film again showed atelectasis of the middle lobe of the right lung, which subsequently cleared up without bronchoscopic aspiration (fig. 4 *A*). The roentgen appearance in June 1937 is shown in figure 4 *B*.

CASE 3.—(This case is presented through the permission of Dr. Eugene T. McEnery.) J. M., a girl 6 years old, was admitted to the Children's Memorial Hospital in January 1936 with a history of a nasal discharge and cough of four days' duration. Her temperature was 103 F., and she had vomited just before

admission. She had a history of asthma in the winter and hay fever in the summer. Cutaneous tests had previously shown her sensitive to ragweed, marsh elder, redtop and a few foods. She had a positive family history for allergy in that her father had suffered with pollinosis and asthma since his childhood. She had had poliomyelitis two years before. The physical examination revealed the residual paralysis of the poliomyelitis, and auscultation of the chest showed bronchial breathing and a few rales over the upper lobe of the right lung. On the following day there were more rales throughout both lungs, and it was thought that the

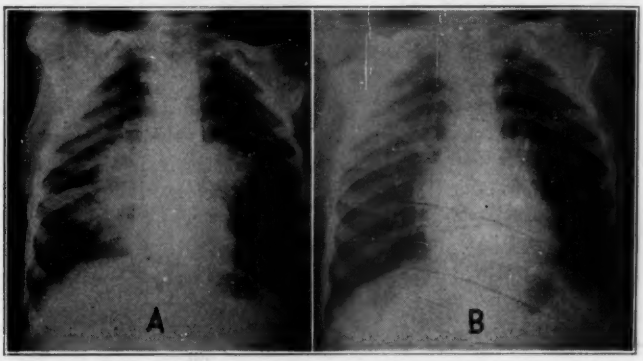

Fig. 4 (Case 2).—Roentgenograms of the same patient taken: *A*, during a second attack three months after the first, and *B*, two days later.

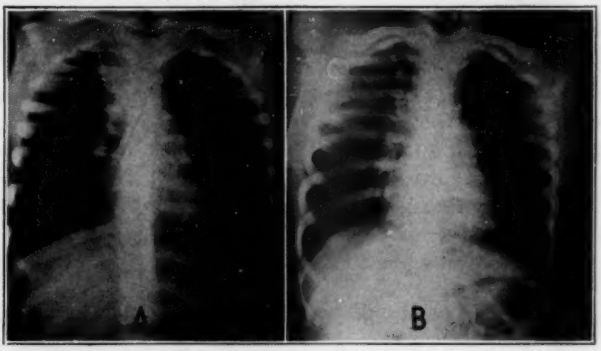

Fig. 5 (Case 3).—Roentgen appearance: *A*, on the patient's admission to the hospital; *B*, two days later.

breath sounds were more audible in the upper lobe of the right lung than on the day before. The roentgen diagnosis was atelectasis of the upper lobe of the right lung (fig. 5 *A*). The leukocyte count was 9,200, with 71 per cent neutrophils, 25 per cent lymphocytes, 2 per cent monocytes and 2 per cent eosinophils. The urine was normal.

On the second day the temperature was normal, and the child was clinically well. She has since moved away from Chicago, and there has been no recurrence (fig. 5 *B*).

CASE 4.—H. P., a 4 year old girl, was first seen in the outpatient department of the Children's Memorial Hospital in 1932. The past history showed that she had had severe eczema since the age of 6 months, with recurrence at varying intervals since that time and asthma of three years' duration.

The tuberculin test was negative. The blood count was normal except that there were 16 per cent eosinophils. A roentgenogram of the chest showed an accentuation of the hilar markings compatible with chronic bronchitis. The allergic investigation at the time consisted of a few scratch tests.

The child dropped out of the clinic for about five years and was not seen again until January 1938. She had had severe asthma and recurrent eczema since her last visit. Examination revealed barrel chest, dyspnea and orthopnea. She was extremely undernourished and underdeveloped. The heart was normal. The lungs were filled with asthmatic rales. There were reddened lichenified areas in the cubital and popliteal fossae and about the wrists and ankles. The leukocyte count was 14,000, with 22 per cent eosinophils. The nasal smear contained a few eosinophils. On allergic investigation, positive reactions were found to wheat, egg, chocolate, cottonseed, silk, feathers and camel, dog and cat hairs as well as to grass and weed pollens.

On April 14 the patient became severely ill at home and was hospitalized at another institution. The roentgen films taken at that time revealed a shadow along the transverse fissure of the right lung, which was diagnosed as an interlobar effusion but which failed to show any thickened pleura (fig. 6 *A*). Roentgen therapy was administered. Seven days later films taken in the roentgen department of the Children's Memorial Hospital showed that the shadow had entirely disappeared (fig. 6 *B* and *C*). On review of these films, the diagnosis of interlobar effusion was changed to atelectasis of the posterior division of the upper lobe of the right lung.

CASE 5.—I. G., a 12 year old boy, was brought to the Children's Memorial Hospital in the fall of 1935 with the complaint of sneezing and a profuse nasal discharge. His past history revealed that he had had an adenoidectomy and tonsillectomy in 1931, asthmatic attacks every fall and through the winter and perennial nasal symptoms with an exacerbation in the summer. The family history was positive for allergy in that his mother had asthma and hay fever, his brother had eczema, and his maternal grandmother was asthmatic. A few cutaneous tests were done, and he was found sensitive to timothy, ragweed and cat and dog hair.

He was admitted to the hospital on Dec. 29, 1937, with a history of an asthmatic attack on December 23, with an exacerbation of symptoms associated with fever three days later. The night prior to admission, he suffered from abdominal pain, fever and nausea. Examination revealed impairment of the percussion note and moist rales over the base of the right lung posteriorly. There was prolongation of the expiratory phase, and the heart was slightly displaced to the right (fig. 7 *A*). There was suppression of normal breath sounds over the lower lobe of the right lung, with dry rales and an occasional wheeze on both sides. His temperature was 100.8 F. on admission and remained slightly elevated for seven days. The findings of dulness, suppression and rales at the base of the right lung continued, but the wheeze and the dry rales disappeared. On the ninth day of hospitalization bronchoscopic aspiration revealed red and swollen mucosa. Thick,

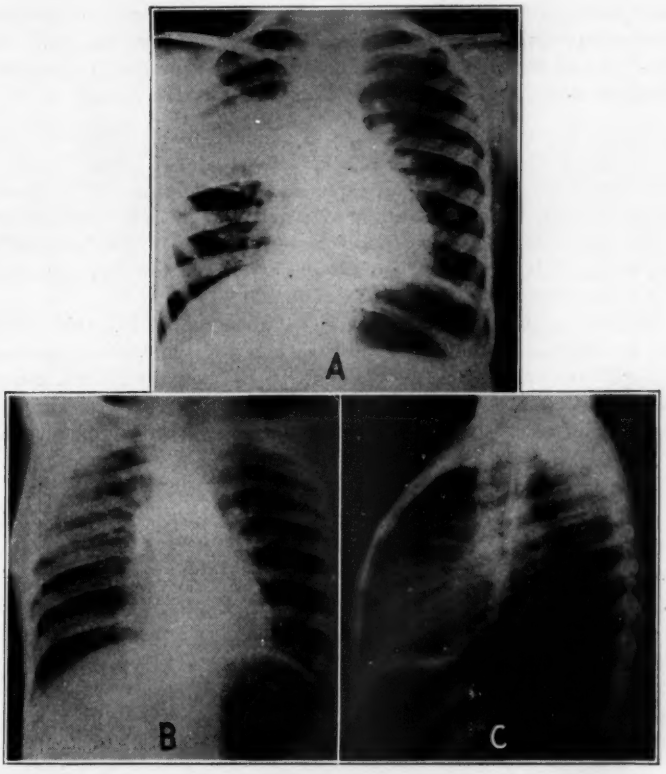

Fig. 6 (Case 4).—Roentgenograms taken: *A*, during the height of symptoms; *B* and *C*, eleven days later.

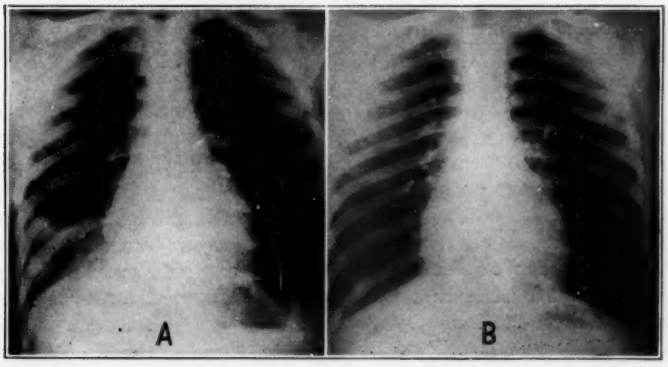

Fig. 7 (Case 5).—Roentgen appearance: *A*, when the patient was admitted to the hospital; *B*, twelve days later, after bronchoscopy.

tenacious mucus was obtained from the lower bronchus on the right side. No eosinophils were found in this secretion. After bronchoscopy, the wedge-shaped shadow that the roentgenogram had revealed largely disappeared (fig. 7 *B*). The tuberculin test was negative. The blood count showed 4 per cent eosinophils.

A complete allergic study of this boy is now in progress.

CASE 6.—J. W., a girl 7 years old, was admitted to the Children's Memorial Hospital in April 1935 with a history of asthma of two years' duration. She had had a severe cough for the past three weeks, accompanied by an intermittent pain in the left side during the attacks of coughing. This pain had become more severe and more constant during the past four days, and the temperature was slightly elevated. The patient had asthma and hay fever. She had a family history of allergy in that her mother suffered from bronchial asthma.

The physical examination revealed a temperature of 101 F., rapid and shallow breathing and enlarged and inflamed tonsils. There were dulness and suppression of normal breath sounds over the lower lobe of the left lung posteriorly. No wheezes or rales were present, and the heart was normal. Roentgen films revealed that the heart was shifted to the left with a dense triangular shadow behind it (fig. 8 *A*).

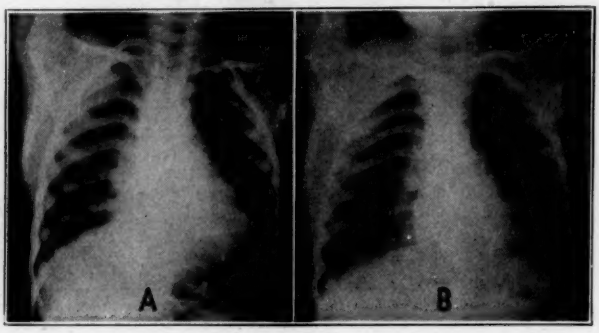

Fig. 8 (Case 6).—Roentgenograms taken: *A*, on admission of the patient to the hospital; *B*, three weeks later.

The tuberculin test was negative. The red cell count was 5,000,000, with 75 per cent hemoglobin; the white cell count was 22,600, and the nasal smear showed a moderate number of eosinophils. The urine was normal.

The chest cleared up rapidly following postural drainage. Soon after admission, the patient coughed up a plug of thick mucus and immediately following this, rales and breath sounds were heard over the previously collapsed lobe. The chest was entirely clear on her discharge (fig. 8 *B*).

Since that time, the patient has been followed in the allergy clinic. Cutaneous tests revealed positive reactions to milk, egg, apple, banana, orange, string beans, rabbit hair, red top, timothy and orchard and blue grass. With a milk-free diet her asthma has been controlled, and she is receiving hyposensitization injections for her pollinosis with good results.

CASE 7.—G. O., a boy, was first seen at the age of 8 months because of eczema and asthmatic wheezes throughout both lungs. He did not attend the clinic and was not seen again until July 1937, four and a half years later, when there was a complaint of a persistently large abdomen and enuresis. Examination gave

entirely negative results except for a large cystlike mass in the left side of the abdomen, which was diagnosed as a huge hydronephrosis. The lungs were clear, and the urine and blood were normal. The Mantoux, Wassermann and Kahn tests were negative. The past history showed that the child had had asthmatic attacks since infancy. He had a family history of allergy in that his father had had bronchial asthma since childhood.

The boy was operated on, and a mass 17 cm. in length was removed after 1,150 cc. of urine had been aspirated from it. On the third postoperative day a cough and dyspnea developed, and the chest showed flatness, bronchial breathing, suppression and rales on the right side, with the heart pulled far to the right

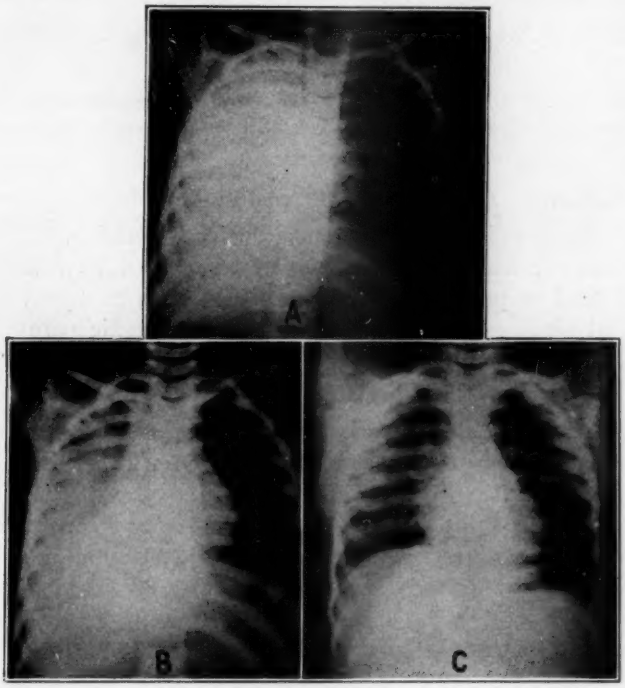

Fig. 9 (Case 7).—Roentgenograms taken: *A*, three days after operation; *B*, six days postoperatively, one day after bronchoscopy; *C*, one month later.

(fig. 9*A*). The temperature continued between 103 and 104 F., and on the sixth postoperative day bronchoscopic examination was done by Dr. Holinger, who noted: "Large amounts of tenacious, purulent material aspirated from the right side. Very little secretion on the left. The mucosa was not markedly inflamed."

The temperature dropped to 100 F. and subsequently remained normal (fig. 9*B*). The bronchi were aspirated twice again, and on discharge the child was clinically well and roentgenograms were normal (fig. 9*C*). Three months later the patient returned to the clinic with a true asthmatic attack. The differential blood count revealed 16 per cent eosinophils. The child is now being completely tested.

ETIOLOGY

The etiology of atelectasis has been the subject of numerous papers, both teleologic and experimental. The earliest of the theories was that of postinfectious (diphtheritic) diaphragmatic paralysis, advanced by Pasteur.[11] More recently there have been the hypoventilation theory, advanced by Henderson,[12] the theory of bronchial occlusion, by Coryllos and Birnbaum,[13] and others.

The processes which may conceivably produce bronchial obstruction in a person with allergy have been summarized by Miller and his associates,[8] as follows:

1. Spasm of the bronchial musculature producing bronchial constriction.

2. Thickening of the walls of the bronchi and bronchioles from edema, hyperplasia, hypertrophy and cellular infiltration, as described in pathologic reports.

3. Secretion of a very thick and tenacious mucus.

4. Paradoxic collapse of the bronchi during expiration. All of these factors fit in well with the most tenable theory, that of bronchial obstruction, and tend to produce the additional condition of hypoventilation, as the tidal air is greatly reduced during an asthmatic paroxysm.

TREATMENT

The treatment of atelectasis is twofold. One is concerned first with the immediate relief of the patient and second with methods of preventing recurrence.

Treatment is directed at removing the mucous plug from the bronchus. The ordinary indirect methods are postural drainage and the use of expectorants and drugs which increase the bronchial secretion or render it more liquid. Epinephrine hydrochloride given subcutaneously, while it makes the patient more comfortable, does not serve to release the tenacious, thick mucoid plugs. If the condition persists, we believe that immediate bronchoscopic aspiration is the method of choice, and the aspiration may have to be repeated until the pulmonary tree is free of obstruction.

In preventing recurrence the physician must determine, if possible, by means of a thorough allergic study the cause of the asthmatic attacks and by preventing the seizures eliminate recurrences of the atelectasis.

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COMPLICATIONS AND SEQUELAE

The importance of atelectasis, irrespective of its cause, as a factor in the production of bronchiectasis was discussed by Anspach [14] and by Boyd.[15] The mechanics of the development of bronchiectasis subsequent to atelectasis were thoroughly presented in Andrus'[16] paper. Clerf [17] recently described a close association between bronchial asthma and bronchiectasis. Watson and Kibler [18] reported cases of bronchiectasis occurring in allergic persons and expressed the opinion that the pathologic condition in these persons is on an allergic basis; they found these persons helped by a regimen directed toward the control of the allergic symptoms.

SUMMARY AND CONCLUSIONS

Six cases of nontraumatic, nonpostoperative atelectasis and 1 case of postoperative atelectasis occurring in allergic children are reported.

The processes in bronchial asthma which may produce bronchial occlusion are bronchospasm, thickening of the bronchial walls, secretion of thick mucus and paradoxic collapse of the bronchi during expiration. All evidence seems to point to bronchial occlusion as the principal cause of atelectasis.

The diagnosis and the treatment of atelectasis occurring during an asthmatic paroxysm are discussed.

The possibility of recurrent atelectasis as a precursor of bronchiectasis is presented.

The prevention of recurrent atelectasis in sensitive persons by adequate allergic control and treatment is considered.

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CIRCULATORY FUNCTION IN THE ANEMIAS OF CHILDREN

IV. ROENTGENOGRAPHIC MEASUREMENT OF CARDIAC SIZE

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Cardiac enlargement is perhaps the most certain single sign of heart disease. Important information might be added to studies of cardiac function in anemic children if it were possible to demonstrate significant changes in the size of the heart before and after treatment of a disorder of the blood. Roentgen examination, provided that a careful technic is used and that its fallacies are completely understood, is the most satisfactory means of obtaining such measurements. It is more accurate than clinical methods, and permanent records are obtained which may be kept for comparison. There is the added advantage that they may be interpreted by more than one observer.

Recently several writers have pointed out the value of roentgenkymography in the study of heart disease,[1] and it seemed that this technic might be useful in the present investigation. Since exercise is an important test of cardiac efficiency, we reasoned that we might enhance the value of our data by taking roentgenkymographic tracings before and after exercise. This could be done before and after treatment, and the records thus obtained could be compared with those for normal children.

Dr. Parsons' work was done during the tenure of the Walter Myers Travelling Studentship.

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1. (*a*) Stumpf, P.: Die Gestaltänderung des schlagenden Herzens im Röentgenbild, Fortschr. a. d. Geb. d. Röntgenstrahlen **38**:1055, 1928; X-Ray Kymography of the Heart, Brit. J. Radiol. **7**:707, 1934. (*b*) Hirsch, I. S.: The Recording of Cardiac Movements and Sounds by the Roentgen Ray, Radiology **22**:403, 1934; The Application of Roentgenkymography to Diagnosis of Cardiac Disease, ibid. **23**: 720, 1934; Examination of the Heart by the Roentgenkymographic Method, Brit. J. Radiol. **7**:728, 1934. Hirsch, I. S., and Gubner, R.: Application of Roentgenkymography to the Study of Normal and Abnormal Cardiac Physiology, Am. Heart J. **12**:413, 1936.

Attempts to calculate cardiac output by roentgenographic methods have been made from time to time. Johnson [2] used the roentgenkymograph to calculate an index which he held to be roughly comparable to the stroke volume of the heart as determined by Hamilton's dye technic.[3]

The following questions define the scope of our investigation:

1. Does treatment cause any change in the size of the heart of the anemic child as determined by roentgen methods?

2. What change, if any, occurs in the roentgenkymographic tracing of the normal child in response to a standard amount of exercise?

3. What change is produced in the tracing of the heart of the anemic child in like circumstances?

4. How does treatment modify the response of the anemic child to exercise?

5. Is it possible by applying the roentgenkymographic index to form even a rough idea of the variations in stroke volume which are caused by exercise and treatment?

MATERIALS

Clinical Material.—Our efforts to answer these questions were concentrated on 5 anemic patients, whose case records have been previously summarized.[4] In addition, 10 convalescent children who were known to be free from cardiac, respiratory and blood diseases were chosen as controls. Their ages ranged from 6 to 12 years. Five were convalescent from operations (herniotomy, mastoidectomy and repair of hypospadias), 2 were awaiting elective operations, 1 had diabetes mellitus, and 1 had recovered from nephrosis and was free from edema and hypertension.

Apparatus.—For details of the construction and operation of the roentgenkymograph the papers of Stumpf [1a] and of Hirsch [1b] should be consulted. In brief, it consists of a roentgen ray tube, a grid formed of parallel lead strips 12 mm. wide, with a space of 1 mm. between strips, and a photographic plate arranged to fall exactly 11 mm. at a constant rate during the exposure. We used an exposure of one to one and one-half seconds.

In passing from the tube to the film, the roentgen rays traverse first the patient and then the grid. All the rays except those which coincide with the slits in the grid are filtered out by the lead. An exposure on a stationary film, therefore, would reveal only a series of narrow sections of the chest, each 1 mm. wide and separated from its neighbor by 12 mm. The descent of the film through 11 mm., however, produces a vertical line of this length at any point of junction between contrasting

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2. Johnson, S. E.: Roentgenkymography Considered in Relation to Heart Output and a New Heart Index, Am. J. Roentgenol. **37**:167, 1937.

3. Hamilton, W. F.; Moore, J. W.; Kinsman, J. M., and Spurling, R. G.: Simultaneous Determinations of the Pulmonary and Systemic Circulation Times in Man and of a Figure Related to Cardiac Output, Am. J. Physiol. **84**:338, 1928.

4. Parsons, C. G., and Wright, F. H.: Circulatory Function in the Anemias of Children: I. Effect of Anemia on Exercise Tolerance and Vital Capacity, Am. J. Dis. Child. **57**:15 (Jan.) 1939.

densities. These lines are straight in the case of points such as those of the spine and humerus and (when the breath is held) of the ribs and diaphragm, and wavy in the case of points which are in motion, such as those of auricles, ventricles and great vessels. The latter may be differentiated by the character of the waves they produce. The troughs of the waves when joined outline the heart in systole, while the crests correspond to diastole. It must be borne in mind constantly that the film records not the whole chest but rather 1 mm. serial sections spaced at intervals of 12 mm. The type of apparatus which we used traces the waves from below upward in each section, and a timer measuring intervals of one fifth of a second records the speed at which the plate moves.

METHODS

With our equipment it was not practicable to use the standard teleroentgenographic target-film distance of 2 meters. The 30 inch (76 cm.) interval commonly used with the roentgenkymograph had to be employed, and, in order to preserve uniformity, it was necessary to expose the plain films also at this distance. These films were held in the roentgenkymograph with the grid removed. The use of a short target-film distance undoubtedly increases the dimensions of the cardiac shadow, but this is unimportant, since we were concerned with relative rather than absolute values.

Films were taken in each case with the patient in the posteroanterior and left anterior oblique position. The order of procedure was first to take the plain roentgenograms, each with an exposure of half a second; the grid was then placed in position, and the kymograms were taken in the posteroanterior and left anterior oblique projections. After exercise kymograms were again made, and as the apparatus was already adjusted to hold the patient in the oblique position, the oblique view was taken first, so that time was saved in making all the exposures. The standard exercise consisted of the ascent of three flights of stairs at a constant pace. This amounted approximately to a rise of 30 feet (9 meters) in one minute, although an exception had to be made in case 2 before transfusion, the child in this case climbing only one flight.

Control of Position.—Since interpretation of results depends in large measure on ability to obtain film records with the subject in exactly the same position at successive examinations, we were forced to devise a method by which the position could be fixed and later duplicated. This was done in taking the posteroanterior views by pressing the chest and shoulders firmly aganist the grid, where they were held by one of us. The feet were maintained in position in the manner to be described. We recognize that it was difficult to reproduce the oblique position, but we concluded that if the feet and shoulders were fixed and if the subject were made to stand erect, scoliosis, kyphosis and twisting of the trunk would be eliminated. An apparatus was constructed to achieve this. A sliding arm, from which were suspended adjustable shoulder braces, was attached to the stand supporting the grid. The arm was so calibrated that the position of all the parts could be accurately recorded and duplicated. The placing of the child's feet was controlled by tracing their outline on a piece of paper which bore a fixed relation to the base of the apparatus. On reexamination the subject simply stepped back into his footprints. The oblique views were taken with the frontal plane of the subject at an angle of 50 degrees to the film, for this degree of rotation was usually sufficient to insure that the shadow of the posterior border of the heart was clear of the shadow of the spine.

Comparing and Measuring Films.—Before 2 roentgenograms of the same patient can be justifiably compared, it is necessary to be certain that they are identical in respect to the position of the patient, the phase of respiration and the height of the diaphragm. From the plain roentgenograms tracings were made of the inner wall of the chest, the diaphragm and the heart. By superimposing these tracings in such a way that the bony landmarks, and therefore the apexes of the lungs, coincided, variations in the height of the diaphragm could be recognized and their influence on the width of the heart assessed. This is Palmer's method,[5] which relies on visual impression rather than actual measurement for evaluating changes in cardiac size. For purposes of tabulation, however, we measured the greatest transverse cardiac diameters by the usual methods.

The roentgenkymograms were treated in a somewhat similar manner. In each bar points were plotted which corresponded with the inner wall of the chest, the diaphragm and the systolic and diastolic borders of the heart. These points were then joined by a smooth freehand curve, and the tracings produced could be superimposed or measured in the same way as those derived from the plain films. When there had been no motion of the bony thorax or diaphragm, the film presented cardiac waves of uniform breadth in each bar. When slight movement had occurred, there was some irregularity of the waves, and in such a case points were taken only from the upper wave complex in each bar. The points obtained were therefore synchronous. Transverse diameters were also measured from the films recording oblique views, but since there are no well defined standards for computing the diameters in the oblique position, the area of the ventricular silhouette was calculated. This was done by transferring to graph paper that portion of the tracing which showed ventricular waves and counting the squares enclosed in the outline. These measurements of area were used only to check the validity of the transverse diameters. The cardiac rate was calculated from each of the kymographic plates.

Calculation of the Roentgenkymographic Index.—This value was obtained after the method of Johnson.[2] The chart shows the scheme of calculation. The left ventricle is assumed to be a cylinder. The total transverse diameter (TR) is measured on the posteroanterior kymogram. On the basis of a series of postmortem observations, the width of the left ventricle in full diastole (VDD) is assumed to be 0.6 times TR. The transverse diameter at the end of systole is derived by measuring the excursion of the left ventricular border in each bar in which it is visible and taking the mean value, the ventricular thrust (VT). Since an equal degree of contraction is assumed to take place along the unseen border of the ventricle on the right, VDS equals $VDD - 2VT$. The height of the ventricle (ALT) is determined by measuring the distance along the left cardiac border over which ventricular pulsations are visible. Then, since the volume of a cylinder equals $\pi r^2 h$, the stroke volume may be roughly calculated as $ALT\ (\pi\, VDD^2/4 - \pi\, VDS^2/4)$. Johnson admitted that this index does not correspond strictly to the stroke volume.

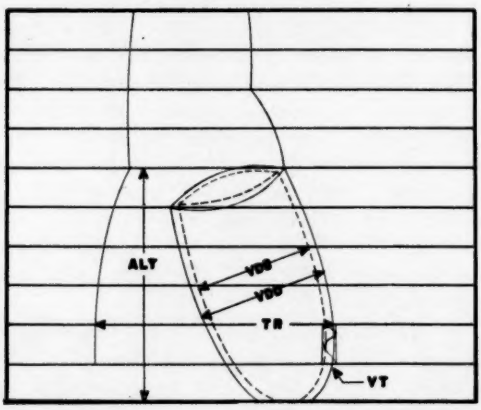
RESULTS

The measurements obtained by the procedure outlined are presented in tables 1 to 4. Table 1 shows the greatest transverse diameters (TD) obtained from the plain films of the hearts of control subjects. Measure-

5. Palmer, J. H.: The Development of Cardiac Enlargement in Diseases of the Heart: A Radiological Study, Medical Research Council, Special Report Series, no. 222, London, His Majesty's Stationery Office, 1937.

ments made from the kymographic films before and after exercise are included. The two columns labeled "D" and "S" refer respectively to the transverse diameters in diastole and systole. The pulse rate and roentgenkymographic index are recorded in each instance. Table 2 contains similar measurements taken from films of the control subjects in the left anterior oblique position; measurements of ventricular area are not included but parallel those of the diameters. We were unable to devise a satisfactory method of calculating a roentgenkymographic index from the oblique films. Tables 3 and 4 contain similar data on the anemic subjects both before and after transfusion. Determinations of hemoglobin concentration have also been included.

If the results obtained and charted in the tables accurately represent the variations in cardiac size under the conditions of the experiment,



Johnson's method of computing the roentgenkymographic index. *ALT* indicates the height of the ventricle; *TR*, the total transverse cardiac diameter; *VDS*, the diameter of the left ventricle during systole; *VDD*, the diameter of the left ventricle during diastole, and *VT*, the thrust of the left ventricle. For a fuller explanation see the text.

then the answers to the questions which we propounded in an earlier part of this paper are as follows:

1. The hearts of anemic children tend to decrease in size as a result of transfusion. This diminution in the transverse diameter of the resting heart was seen in all 5 posteroanterior views and in 4 of the 5 oblique views. The decreases varied from 0.2 to 3.3 cm.

2. In the majority of normal children exercise is followed by immediate reduction in the size of the heart. In the posteroanterior view the diameter was shortened in 8 cases, lengthened in 1 and unchanged in 1. In the oblique position 7 hearts decreased, 2 increased and 1 did not vary. The variation ranged from + 0.2 to — 1.2 cm.

TABLE 1.—*Measurements of Posteroanterior Films of Controls* *

Patient	Age, Yr.	TD, Cm.	Roentgenkymograms Before Exercise				Roentgenkymograms After Exercise				D′ — TD, Cm.	S′ — TD, Cm.	D″ — D′, Cm.	S″ — S′, Cm.	P‴ — P′	RKGI‴ — RKGI′
			D′, Cm.	S′, Cm.	P′	RKGI′	D″, Cm.	S″, Cm.	P‴	RKGI‴						
A. C.	9	9.9	10.9	9.8	73	67	10.8	9.9	73	72	+1.0	—0.1	—0.1	+0.1	0	+ 5
F. W.	10	9.1	11.1	10.5	100	68	10.1	9.2	110	75	+2.0	+1.4	—1.0	—1.3	+10	+ 7
E. W.	8	9.4	10.4	9.7	145	53	10.2	9 3	157	63	+1.0	+0.3	—0.2	—0.4	+12	+10
F. S.	9	9.4	11.1	10.3	91	76	(10.7)	(9.9)	95	(76)	+1.5	+0.9	(—0.4)	(—0.4)	+ 4	(0)
S. B.	7	10.3	(12.6)	(11.8)	78	(70)	11.4	10.5	72	73	+2.3	+1.5	(—1.2)	(—1.3)	— 6	(+ 3)
G. H.	8	9.9	9.7	9.1	100	45	9.9	9.1	85	51	—0.2	—0.8	+0.2	0	—15	+ 6
R. A.	6	7.7	8.5	8.1	110	31	8.2	7.7	137	33	+0.8	+0.4	—0.3	—0.4	+27	+ 2
S. B.	12	10.6	11.7	11.0	91	74	(11.2)	(10.6)	110	(72)	+1.1	+0.4	(—0.5)	(—0.4)	+19	— 2
A. S.	6	8.4	8.6	7.8	78	34	8.6	8.0	85	41	+0.2	—0.6	0	+0.2	+ 7	+ 7
R. C.	7	9.4	(10.4)	(9.8)	137	(61)	10.2	9.6	110	43	+1.0	+0.4	(—0.2)	(—0.2)	—27	(—18)
										Mean	+1.07	+0.38	—0.34	—0.41	+ 3.1	+ 2

* In tables 1 to 4, TD indicates transverse cardiac diameter estimated from plain films; D, maximum diameter from kymograms; S, minimum diameter from kymograms; P, pulse rate; RKGI, roentgenkymographic index. Figures in parentheses denote readings from technically imperfect films.

TABLE 2.—*Measurements of Oblique Films of Controls*

Patient	Age, Yr.	TD, Cm.	Roentgenkymograms Before Exercise			Roentgenkymograms After Exercise			D′ — TD, Cm.	S′ — TD, Cm.	D″ — D′, Cm.	S″ — S′, Cm.	P‴ — P′
			D′, Cm.	S′, Cm.	P′	D″, Cm.	S″, Cm.	P‴					
A. C.	9	11.4	10.2	9.0	73	(9.9)	(8.7)	110	—1.2	—2.4	(—0.3)	(—0.3)	+37
F. W.	10	8.5	10.2	9.0	91	(9.5)	(8.4)	137	+1.7	+0.5	(—0.7)	(—0.6)	+46
E. W.	8	9.6	10.3	9.3	105	9.9	8.9	139	+0.7	+0.3	—0 4	—0.4	+34
F. S.	9	8.9	9.4	8.6	105	9.6	8.6	157	+0.5	—0 3	+0.2	0	+52
S. B.	7	9.9	11.1	9.7	85	11.1	9.3	130	+1.2	—0.2	0	—0.4	+45
G. H.	8	8.6	10.1	8.5	88	(9.8)	(8.1)	101	+1.5	—0.1	(—0.3)	(—0.4)	+13
R. A.	6	7.4	8.5	7.7	122	8.2	7.4	137	+1.1	+0.3	—0.3	—0.3	+15
S. B.	12	9.1	10.7	9.6	105	10.3	9.2	157	+1.6	+0.5	—0.4	—0.4	+52
A. S.	6	8.7	8.9	8.0	59	8.3	6.9	65	+0.2	—0.7	—0.6	—1.1	+ 6
R. C.	7	9.0	(9.9)	(9.1)		(10.0)	(9.1)		+0.9	+0.1	(+0.1)	(0)	
								Mean	+0.87	—0.21	—0.27	—0.39	+33.3

TABLE 3.—*Measurements of Posteroanterior Films of Anemic Patients*

	Age, Yr.	Hemoglobin, Content, Gm.	TD, Cm	Roentgenkymograms Before Exercise				Roentgenkymograms After Exercise				D′ — TD, Cm.	S′ — TD, Cm.	D″ — D′, Cm.	S″ — S′, Cm.	P″ — P′	RKGI″ — RKGI′
				D′, Cm.	S′, Cm.	P′	RKGI′	D″, Cm.	S″, Cm.	P″	RKGI″						
Case 1																	
Before transfusion	7	5.1	(11.1)	10.5	10.0	131	37	10.7	10.1	129	62	(—0.6)	(—1.1)	+0.2	+0.1	— 2	+25
After transfusion..	7	9.7	(10.4)	10.5	9.8	96	43	(11.0)	(10.2)	86	(57)	(+0.1)	(—0.6)	(+0.5)	(+0.4)	—10	(+14)
Change in case 1		+4.6	(—0.7)	0	—0.2	—35	+6	(+0.3)	(+0.1)	—43	(—5)						
Case 2																	
Before transfusion	7	2.4	14.5	15.1	14.6	129	109	15.0	14.4	147	107	+0.6	+0.1	—0.1	—0.2	+18	— 2
After transfusion..	7	9.5	12.7	12.5	11.9	114	67	(13.7)	(12.9)	114	(101)	—0.2	—0.8	(+1.2)	(+1.0)	0	(+34)
Change in case 2		+7.1	—1.8	—2.6	—2.7	—15	—42	(—1.3)	(—1.5)	—33	(—6)						
Case 3																	
Before transfusion	7	6.6	13.7	14.1	13.7	122	38	13.8	13 4	129	49	+0.4	0	—0.3	—0.3	+ 7	+11
After transfusion..	7	8.0	13.0	13.5	13.1	91	70	13.7	13.2	79	68	+0.5	+0.1	+0.2	+0.1	—12	— 2
Change in case 3		+1.4	—0.7	—0.6	—0.6	—31	+32	—0.1	—0.2	—50	+19						
Case 4																	
Before transfusion	4	6.3	10.0	9.8	9.5	114	40	10.4	9.6	103	36	—0.2	—0.5	+0.6	+0.1	—11	— 4
After transfusion..	4	13.8	9.7	10.1	9.6	87	39	10.2	9.6	73	51	+0.4	—0.1	+0.1	0	—14	+12
Change in case 4		+7.5	—0.3	+0.3	+0.1	—27	—1	—0.2	0	—30	+15						
Case 5																	
Before transfusion	5	6.8	9.0	9.4	8.9	128	33	8.9	8.2	147	35	+0.4	—0.1	—0.5	—0.7	+19	+ 2
After transfusion..	5	12.8	8.8	9.0	8.5	108	30	8.9	8.4	116	35	+0.2	—0.3	—0.1	—0.1	+ 8	+ 5
Change in case 5		+6.0	—0.2	—0.4	—0.4	—20	—3	0	+0.2	—31	0						

TABLE 4.—*Measurements of Oblique Films of Anemic Patients*

	Age, Yr.	Hemoglobin, Content, Gm.	TD, Cm.	Roentgenkymograms Before Exercise			Roentgenkymograms After Exercise			D′ — TD, Cm.	S′ — TD, Cm.	D″ — D′, Cm.	S″ — S′, Cm.	P″ — P′
				D′, Cm.	S′, Cm.	P′	D″, Cm.	S″, Cm.	P″					
Case 1														
Before transfusion	7	5.1	(8.6)	10.1	8.8	114	10.5	9.5	141	(+1.5)	(+0.2)	+0.4	+0.7	+27
After transfusion	7	9.7	(9.6)	10.3	9.1	86	10.3	9.2	99	(+0.7)	(—0.5)	0	+0.1	+13
Change in case 1		+4.6	(+1.0)	+0.2	+0.3	—28	—0.2	—0.3	—42					
Case 2														
Before transfusion	7	2.4	14.2	14.0	13.6	137	13.8	13.1	158	—0.2	—0.6	—0.2	—0.5	+21
After transfusion	7	9.5	10.9	11.6	10.7	114	11.4	10.6	129	+0.7	—0.2	—0.2	—0.1	+15
Change in case 2		+7.1	—3.3	—2.4	—2.9	—23	—2.4	—2.5	—29					
Case 3														
Before transfusion	7	6.6	13.0	13.6	12.8	129	13.7	12.9	158	+0.6	—0.2	+0.1	+0.1	+29
After transfusion	7	8.0	12.2	13.1	12.4	91	13.0	12.1	114	+0.9	+0.2	—0.1	—0.3	+23
Change in case 3		+1.4	—0.8	—0.5	—0.4	—38	—0.7	—0.8	—44					
Case 4														
Before transfusion	4	6.3	9.6	9.7	8.5	114	(9.7)	(8.8)	147	+0.1	—1.1	(0)	(+0.3)	+33
After transfusion	4	13.8	9.4	10.2	9.1	103	(9.8)	(8.7)	103	+0.8	—0.3	(—0.4)	(—0.4)	0
Change in case 4		+7.5	—0.2	+0.5	+0.6	—11	(+0.1)	(—0.1)	—44					
Case 5														
Before transfusion	5	6.8	(7.8)	8.9	8.0	128	(8.6)	(7.7)	147	(+1.1)	(+0.2)	(—0.3)	(—0.3)	+19
After transfusion	5	12.8	(7.5)	8.6	7.5	128	8.7	7.3	128	(+1.1)	(0)	+0.1	—0.2	0
Change in case 5		+6.0	(—0.3)	—0.3	—0.5	0	(+0.1)	(—0.4)	—19					

3. Cardiac measurements of anemic children show no constant response to exercise. The posteroanterior roentgenkymograms showed diminution in 3 and enlargement in 2 cases. In the oblique position 2 hearts increased, 2 became smaller and 1 remained the same. The variation ranged from + 0.6 to — 0.6 cm.

4. After transfusion anemic children still have no consistent response to exercise; roentgenkymograms taken with the subjects in the posteroanterior position revealed a greater diameter after exercise in 4 instances and a reduced diameter in 1. The oblique views showed that the cardiac size decreased in 3 patients, increased in 1 and was unaltered in 1.

5. Judged by the roentgenkymographic index, the amount of exercise to which the children were subjected produced an augmented stroke volume in 7 of 10 controls. In 3 of the 5 anemic patients a similar increase in stroke volume as a response to exercise was seen before transfusion, and in 4, after transfusion. If it is true that the roentgenkymographic index varies with the ventricular stroke volume, then when it is multiplied by the pulse rate a figure proportional to cardiac minute volume will result. The application of this calculation to the indexes previously noted produces little change in the proportion of children who responded to exercise with an increased flow of blood.

All these conclusions, however, must remain tentative until the accuracy of the figures on which they are based has been determined. In order to establish this point we must examine the methods by which the figures were obtained.

CRITICAL EVALUATION OF THE METHOD

Roesler [6] stated that unless the bony landmarks and the diaphragm can be directly superimposed and the heart photographed at exactly the same point in its cycle, no comparison of cardiac measurements made from roentgenograms is justified. The technical difficulties involved in obtaining such films are perhaps not generally realized. "Only when careful criteria are fulfilled, are statements referring to changes in size of the cardiovascular silhouette acceptable. Recourse to the majority of publications on this subject reveals much evidence of a vast waste of both energy and material, with concomitant confusion and contradictory results." [6] The criteria which Roesler enumerated will now be set forth, with our efforts to observe them.

1. The target-film distance must be maintained inviolate.

The position of the roentgen ray tube of our apparatus could be exactly reproduced by virtue of a scale on its movable parts. The film holder, though movable, was placed in a position permanently

6. Roesler, H.: Clinical Roentgenology of the Cardiovascular System, Springfield, Ill., Charles C. Thomas, Publisher, 1937.

marked on the tile floor, and its distance from the tube was verified before each set of films was taken. Its weight was great enough to preclude accidental movement while the patient was being placed in position before it. Some check on the accuracy of the target-film distance is afforded by measuring the width of strips on the film made by the grid. If the cardiac size were altered by parallax, this would be reflected in variation in the width of the grid strips. On none of the films did this exceed 1 per cent.

2. The target, the midline of the patient and the midline of the film must be accurately centered. The deviations must not exceed 1 or 2 cm. for the tube and 3 or 4 cm. for the patient.

The centering of the tube was controlled in the same manner as the target-film distance and was exactly the same during paired determinations, since the apparatus was not touched. It may, however, have varied slightly when films were exposed on different days. The amount of lateral deviation was probably slight. A few of the earlier films showed slight differences in the vertical centering of the tube because the importance of measuring the height of the plate holder was not realized at first.

Accurate centering of the patient in the posteroanterior position was more difficult, as this had to be done by eye. In this respect 2 or 3 films transgressed the 3 or 4 cm. limit set by Roesler. On the other hand, the oblique views, in which centering was controlled mechanically, did not show this fault.

3. The chest must not undergo any change in position, either by rotation or by increase of kyphosis or lordosis.

Our attempts to overcome this source of error have been described in the section entitled "Methods." During the long exposure swaying of the body must be prevented. It is obvious that these faults were not completely eliminated from some of the films.

4. The position of the diaphragm must be identical; not only the respiratory phase but the intra-abdominal content must be remembered in this connection. Exposure ought to be made during the midphase of respiration.

In our young patients this factor was the most difficult of all to standardize, since they could not cooperate well in the matter of respiratory control. This was especially true of the anemic subjects, who were dyspneic and in general slightly younger and less intelligent than the controls. We therefore abandoned our attempts to make exposures during midinspiration and tried to obtain films during full inspiration in all cases. The kymograms show that we were not entirely successful, since diaphragmatic movement and differences in the width of the chest are apparent in some instances.

By exposing the films at the same time of day and so in the same relation to mealtime, differences in the amount of abdominal content were eliminated to a considerable extent. Splenic and hepatic enlargement, when present, did not alter sufficiently between successive exposures to affect the height of the diaphragm.

5. The phase of the cardiac cycle must be identical.

This criterion does not apply to kymographic tracings, in which it is possible to define any point in the cardiac cycle. With plain films of anemic subjects we used a half-second exposure in all but 2 cases and measured the maximum transverse diameter. Hirsch and Schwarzschild [7] stated the belief that this is not, as might be supposed, the full diastolic diameter of the heart. Using an apparatus which is so devised that the action currents of the contracting heart control the moment of roentgen exposure, they obtained films synchronous with the full diastolic phase of the heart. On comparison of such films with others, which had long exposure, they came to the conclusion that the record of the heart obtained by long exposure represents a position intermediate between systole and diastole. We took the opportunity of comparing our plain films with the roentgenkymograms. If the view of Hirsch and Schwarzschild is correct and if, as we supposed, our films were obtained under standard conditions, then the diameters of the plain films should fall between the systolic and diastolic phases of the kymograms. In tables 1 to 4 columns are included which enumerate the differences between the transverse diameters measured from the plain films and the diastolic (D′ — TD) and systolic (S′ — TD) diameters of the corresponding kymograms taken with the subject at rest. At a glance it can be seen that no thoroughly constant relation exists between the three diameters. Consideration of the mean of these differences, however, indicates that the diameters of the plain films tend to lie between the maximum and minimum kymographic diameters, which supports the contention of Hirsch and Schwarzschild. The fact that some of the readings of the plain films fall outside the limits of the kymographic diameters is disturbing, as it points to unrecognized faults in technic.

The majority of our films satisfied the criteria demanded by Roesler, and those which failed exhibited for the most part a lack of reproduction of the phase of respiration or of the exact position of the patient. Superimposition of tracings made from the films enabled us to recognize when proper comparability was lacking but did not allow us to determine accurately the effect produced on cardiac size. The most satisfactory way in which to deal with films that for any reason fail to meet the standards of accuracy required is to reject them. This we have done in reassessing our data.

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7. Hirsch, I. S., and Schwarzschild, M.: Directed Roentgenography of the Thorax, Am. J. Roentgenol. **37**:13, 1937.

Even when completely satisfactory films are used for measurement, errors are bound to arise during the mechanical process of mensuration. These include inaccuracies of tracing, differences of interpretation of kymographic waves and those unavoidable irregularities which occur when discrete points are connected by freehand drawing. To check these sources of error a complete set of tracings, together with measurements from them, was made by each of us, and the results were compared. Readings were recorded to the nearest 0.1 cm., and after obviously faulty interpretations had been reviewed we found that none

TABLE 5.—*Changes in Maximum Transverse Cardiac Diameter in All Films*

Conditions	Increase > 0.2 Cm.		No Change		Decrease > 0.2 Cm.	
	Postero-anterior	Oblique	Postero-anterior	Oblique	Postero-anterior	Oblique
Anemic patients after transfusion, plain roentgenograms	0	1	1	1	4	3
Control subjects after exercise, roentgenkymograms	0	0	5	3	5	7
Untreated anemic patients after exercise, roentgenkymograms	1	1	2	3	2	1
Anemic patients after transfusion, after exercise, roentgenkymograms	2	0	3	4	0	1

TABLE 6.—*Changes in Maximum Transverse Cardiac Diameter in Films of Good Comparability Only*

Conditions	Increase > 0.2 Cm.		No Change		Decrease > 0.2 Cm.	
	Postero-anterior	Oblique	Postero-anterior	Oblique	Postero-anterior	Oblique
Anemic patients after transfusion, plain roentgenograms	0	0	1	1	3	2
Control subjects after exercise, roentgenkymograms	0	0	4	2	2	4
Untreated anemic patients after exercise, roentgenkymograms	1	1	2	2	2	0
Anemic patients after transfusion, after exercise, roentgenkymograms	1	0	3	4	0	0

of the readings differed by more than 0.1 cm. In the comparison of 2 films, then, it is not possible to be sure that a real variation in size exists unless the difference exceeds 0.2 cm.

Reassessment of Data.—When the figures presented in tables 1 to 4 were reassessed, the points just discussed were kept in mind. All imperfect films were excluded from consideration, and changes in diameter of 0.2 cm. or less were neglected. The data presented in tables 5 and 6 summarize the changes in diametric measurements which fulfil these conditions.

COMMENT

The corrected figures indicate that in the majority of cases of severe anemia the size of the resting heart decreases when the anemia is corrected by transfusion (table 5). When measurements are ignored, how-

ever, and the plain films are compared by superimposition in the way suggested by Palmer,[5] it at once becomes apparent that slight differences in the height of the diaphragm are mainly responsible for the variations in the width of the heart. In only 2 cases is it possible to be absolutely certain that diminution in the cardiac shadow took place (posteroanterior films in case 3 and oblique films in case 2). Roesler [8] pointed out that it is unwise to estimate the size of the heart from examination in one plane only. It is obvious that cardiac enlargement is volumetric and not confined to a single plane; it should therefore be apparent in more than one projection. Consequently, although these 2 pairs of films are highly suggestive, we cannot conclude from them with certainty that in anemia the heart may dilate and later recover. It was to guard against the danger of false interpretation of this kind that films were taken recording the left anterior oblique as well as the posteroanterior views. The oblique view was so chosen that it gave good definition of the right and left ventricles and the lower border of the heart. Moreover, when studied in conjunction with the posteroanterior views, it helped to exclude the false impression of cardiac enlargement which may occur when the heart rotates on its own axis and brings into silhouette a wider cardiac diameter.

In normal children (table 5) the effect of exercise was a decrease in the size of the heart in both systole and diastole, or else no significant alteration was found in the measurements. In no instance did the heart become larger as a result of exertion. The accuracy of measurements of the roentgenkymograms is limited because it is impossible to be sure of the position of either the diaphragm or the apex of the lung. When a 12 mm. grid is used, there is a possibility of misjudging by at least 1 cm. the position of each of these structures, since both may be hidden behind lead strips. The consistency of our results for normal subjects is the greatest argument in favor of their relative truth.

Anemic children (table 6) do not respond to exercise in such a consistent manner. One case was noted in which an increase in the diastolic diameter was shown in the posteroanterior view, and another in which an increase was shown in both the systolic and the diastolic diameter, in the oblique view. After transfusion no increase in diameter following exercise was demonstrable.

The roentgenkymographic index as an indication of stroke volume gave results which did not always correspond with our expectations. We believe that its inconsistency in our hands was due to the difficulty of estimating correctly the height of the ventricle (*ALT*). The kymo-

8. Roesler, H.: The Relation of the Shape of the Heart to the Shape of the Chest, with Special Reference to the Anteroposterior Dimensions and the Morphology of Various Normal Heart Types, Am. J. Roentgenol. **32**:464, 1934.

gram records the movements of single points on the cardiac outline, each separated by the width of the lead strips in the grid. The height of the ventricle, as judged from that portion of the film which shows ventricular waves, must therefore be an exact multiple of the distance between the grid spaces, 1.2 cm. Any intermediate measurement is precluded. In addition the diaphragm, unless there is a large gas bubble in the stomach, obscures the lower part of the left cardiac border, so that the ventricular tracing is lost, and the height of the ventricle is correspondingly decreased. Furthermore, unqualified acceptance of the assumption that changes in cardiac output are proportional to changes in the external measurements of the heart is unwarranted. A plunger-like motion of the auriculoventricular septum is an important factor in cardiac output, as is evident in cases of constrictive pericarditis, in which there may be no visible external movement of the heart and yet a normal stroke volume. For these reasons, plus the additional one that the alterations in the index as measured were generally small, we are not willing to draw any conclusions from the figures so calculated. A point of possible significance is the decrease, after transfusion, of the product of the roentgenkymographic index times the pulse rate for 4 of the 5 anemic patients in the resting state. This suggests that a decrease in minute volume follows effective treatment of anemia.

REVIEW OF THE LITERATURE

Enlargement of the heart in chronic anemia is well established on clinical, roentgenologic and pathologic grounds. It is said to be due in part to dilatation and in part to hypertrophy, the former preceding and being more common than the latter.[9] Inadequate nutrition of the myocardium by anemic blood is thought to be responsible for the lack of tone and imperfect contraction of the heart muscle which lead to dilatation. Hypertrophy, on the other hand, is probably a direct consequence of the increased work done by the heart to compensate for the anemia. Hypertrophy is almost certainly irremediable.

It is believed by some clinicians that in certain diseases the heart may dilate and, when the causative factor is removed, return to normal size. Palmer [5] in a recent monograph on cardiac enlargement remarked that dilatation "has been described as a complication of many infectious diseases. Most of the observations have been based on clinical methods that cannot be relied on to yield accurate information concerning small changes in size. Radiological studies are few, chiefly on account of technical difficulties, and until they are available our knowledge must remain inexact." He stated that he considered unconvincing such roentgen evidence as has been advanced to prove that dilatation and recovery

9. Lambie, C. G.: The Functional Pathology of Anemia: IV. The Symptoms and Signs of Anemia, M. J. Australia **2**:423, 1937.

may occur in rheumatic fever and acute nephritis, but he did not comment on cardiac enlargement in anemia. Here again, however, roentgen evidence of dilatation and subsequent recovery is scanty. Ball [10] reported such a case, but as the anemia was secondary to menorrhagia and was treated by removal of a greatly enlarged uterus, it is not possible to exclude variations in the height of the diaphragm as a factor responsible for his finding. Widening of the transverse shadow of the heart due to this cause is not infrequently seen in normal women during pregnancy.[11]

Tung and his associates [12] gave roentgen evidence of recovery from the cardiac enlargement of anemia, and Porter [13] reported a series of cases in which he was able to demonstrate a decrease in the size of the heart following correction of anemia due to hookworm infection.

Our own evidence, although suggestive, is inconclusive. This may perhaps be explained on the ground that, as 4 of the 5 patients had had severe anemia for most of their lives, their cardiac enlargement was predominantly due to hypertrophy. A second factor that must be considered is our use of transfusions in the treatment of anemia, since changes in blood volume may be reflected in alterations of the cardiac dimensions. Eyster and Middleton [14] concluded from studies on adults that changes in cardiac volume following transfusion are insignificant. Previously Meek and Eyster [15] recorded a similar opinion, derived from their work on dogs. They stated: "It is evident . . . that intravenous injections, although in two experiments the fluid injected equalled the original blood volume, did not materially affect the diastolic size of the heart. The results were uniform whether either physiologic saline, 6% acacia in saline or blood was used as the injection fluid." When enlargement occurred, it was transitory and of negligible degree, and it was seen only when transfusion produced a considerable increase of venous pressure. The venous pressure of our patients was measured before and after transfusion, and in only a single instance was there any change—a decrease. Moreover, in every instance there was

10. Ball, D.: Change in the Size of the Heart in Severe Anemia, Am. Heart J. **6**:517, 1931.

11. Roesler, H.: Errors in Cardiovascular Roentgen-Ray Interpretation, Ann. Int. Med. **10**:299, 1936.

12. Tung, C. L.; Bien, W. N., and Ch'u, Y. C.: The Heart in Severe Anemia. Chinese M. J. **52**:479, 1937.

13. Porter, W. B.: Heart Changes and Physiologic Adjustment in Hookworm Anemia, Am. Heart J. **13**:550, 1937.

14. Eyster, J. A. E., and Middleton, W. S.: Cardiovascular Reactions to Hemorrhage and Transfusion in Man, Am. J. Physiol. **68**:581, 1924.

15. Meek, W. J., and Eyster, J. A. E.: The Effect of Plethora and Variations in Venous Pressure on Diastolic Size and Output of the Heart, Am. J. Physiol. **61**:186, 1922.

an interval of at least two days between transfusion and roentgen observations, so that transitory effects, if present, should have subsided.

Clinical experience and work on experimental animals have led in recent years to the conclusion that the heart becomes smaller after exercise. This view has gained wider acceptance since roentgen examination was introduced in the study of cardiac physiology, but some difference of opinion still exists. Deficiences in the technic of exposing films probably account for this disagreement, for, again quoting Roesler: "Following strenuous exercise an identical position of the diaphragm, of the chest, and of the cardiac cycle is rarely obtained." [11]

Faber and Kjaergaard,[16] among others, studied the effect of work on the normal heart, using the roentgenkymogram instead of the teleroentgenogram. Confining themselves to a study of the posteroanterior view, they found that in healthy young adults after moderate exercise there was a decrease in the diameters of the heart in both systole and diastole. They computed the probability of such a finding in normal adults as nearly 100 per cent. Our determinations on control subjects agree in their general trend with these observations. It is possible that we might have obtained more certain confirmation if we had exercised the children more strenuously. Examination of table 1 (posteroanterior views of control subjects) reveals that half of the children showed either a drop or a negligible change in pulse rate after exercise, but in table 2 (oblique views) a rise of pulse rate is invariable. This is no doubt due to the fact that after exercise the oblique views were obtained before the posteroanterior views. The time which elapsed before the anterior views were taken was in some cases sufficient to permit the pulse rate to return to normal. It may well be questioned whether a child's heart, when the pulse rate has fallen to the resting level, can still be under the influence of exercise.

We have been unable to discover any previous roentgen studies on the cardiac response to exercise in anemia. Our figures suggest that in some cases the response is abnormal. One patient (case 1) showed a considerable increase in cardiac size immediately after exercise, a response which was in strong contrast to that of the normal children. Another (case 4) responded in a similar but less pronounced manner. In each instance this response was confirmed in only one projection. After transfusion the hearts responded in a more normal manner. With such slender evidence it is of course impossible to be sure that these findings are of any significance, but taken in conjunction with other evidence of cardiac dysfunction they are suggestive of myocardial defect and probably deserve further study.

16. Faber, B., and Kjaergaard, H.: Kymographic Studies on the Influence of Brief Muscular Work upon Heart Function, Acta med. Scandinav. **89**:537, 1936.

Physiologists have expressed the belief that the heart is larger, especially in diastole, during the actual performance of physical work but that compensation is complete as soon as the strain is removed, so that at the completion of exercise the heart is smaller than normal. Owing to technical difficulties, it is almost impossible to confirm this theory by roentgen study. If it is accepted, our observations on the anemic subjects may be explained by slowness or partial failure of compensation.

Our attempts to measure cardiac output were disappointing. Many observers [17] have remarked on an increase in stroke volume in anemia, but as our patients were unable to cooperate well enough to allow us to employ the more commonly used methods of estimating output, our study had to be confined to consideration of the roentgenkymographic index. This, for reasons which have been advanced, proved of no great assistance. Observations derived from measurements of blood oxygen which have been reported in an earlier paper [18] indicate that these children show considerable augmentation of output.

After transfusion, the general conformation of the ventricular waves seen in the kymograms improved somewhat, both in shape and in amplitude.

SUMMARY AND CONCLUSIONS

With a small number of cases and a technic fraught with the possibility of uncontrollable errors, we should be unwise to attempt any sweeping conclusions. Our observations can be interpreted only as impressions, which must be substantiated by more accurate determinations.

We were unable to prove that the heart which is enlarged as a result of long-standing severe anemia will diminish in volume after treatment. Several plain films showed a reduction in size after transfusion, but in no case was this decrease visible in two planes. Roentgenkymographic measurements in both anterior and oblique views showed that the hearts of 3 patients became smaller after transfusion. Roentgenkymograms give less reliable information than plain roentgenograms, but the evidence certainly suggests that in some cases an actual decrease in cardiac volume takes place.

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17. Fahr, G. E., and Ronzone, E.: Circulatory Compensation for Deficient Oxygen Carrying Capacity of the Blood in Severe Anemias, Arch. Int. Med. **29**: 331 (March) 1922. Richards, D. W., Jr., and Strauss, M. L.: Circulatory Adjustment in Anemia, J. Clin. Investigation **5**:161, 1928. Grollman, A.: The Cardiac Output of Man in Health and Disease, Springfield, Ill., Charles C. Thomas, Publisher, 1932.

18. Parsons, C. G., and Wright, F. H.: Circulatory Function in the Anemias of Children: II. Measurements of Blood Oxygen Content, Circulation Time and Venous Pressure, Am. J. Dis. Child. **57**:330 (Feb.) 1939.

The hearts of normal children responded to exercise by diminishing or remaining unchanged in size. The decrease was not always enough to be significant, and in some instances it is doubtful whether the subjects had performed enough work. In no case did the measurements of the heart increase as a result of exercise.

Anemic children did not respond to exercise in any uniform way; in 1 or 2 instances enlargement of the heart took place after exercise; in other cases there was a decrease or no change. Our impression is that the hearts of some anemic subjects respond to exercise in an abnormal manner.

After treatment of anemia, exercise did not effect any increase in the diameters of the heart; as a general rule the diameters remained unchanged. This evidence suggests that the anemic child's heart responds to exercise in a more normal manner after treatment..

Attempts to estimate stroke volume from the roentgenkymographic index were so replete with possible errors that no conclusions could be drawn.

We were chiefly impressed by the large number of variable factors influencing our measurements and by the difficulty in controlling them adequately. We do not feel that our technic, despite the care taken, was sufficiently exacting to permit accurate observations on the comparatively small changes in cardiac dimensions which occurred. We doubt whether the method can be used to make satisfactory determinations on small or mentally retarded children, and we suspect that even if it were applied to adults giving good cooperation its complexity would preclude any but guarded conclusions.

The roentgenkymograph was obtained through Dr. D. Ball, of the Department of Roentgenology of the Presbyterian Hospital. Technical assistance was contributed by Miss C. McCoy, of the Squier Urological Clinic.

SUMMARY OF OUR STUDIES ON CIRCULATORY FUNCTION

The results of our efforts to evaluate the effect of anemia on the circulatory system of children have been reported in a series of papers.[19] Our objectives were to recognize and assess the lesser degrees of cardiac dysfunction, to form some idea of the cardiac reserve and to observe the degree of improvement which followed alleviation of anemia. In addition, we took the opportunity to study afresh the processes by which the body compensates for anemia. Practically all previous investigations of this kind have been confined to adults; when small children are used as the experimental subjects, accurate study is bound to be difficult. The inability of young patients to cooperate in complicated

19. Parsons, C. G., and Wright, F. H.: Circulatory Function in the Anemias of Children: III. Alterations in the Electrocardiogram, Am. J. Dis. Child. **57:** 851 (April) 1939; footnotes 4 and 18.

procedures precludes the use of many of the well recognized forms of examination and increases the chance of unavoidable errors of method or technic. Such deficiencies could be controlled in some measure by comparing the performances of our subjects with those of normal children of like age under similar conditions. It has to be remembered, however, that the circulatory mechanism is complex, with many variable interlocking physiologic responses, and that no matter how accurate are the observations one cannot assume when examining one response of the cardiovascular system that the others will remain constant. In order to simplify the form of presentation, in each of our previous papers we dealt with an individual aspect of the reaction of the circulation to anemia; it is now our task to review and correlate our findings as a whole.

Cardiovascular Compensation for Anemia.—Anemia diminishes the oxygen-carrying capacity of the blood, and certain physiologic adjustments must take place in order to maintain an adequate supply of oxygen to the tissues. We enumerated in our first paper [4] some of the compensatory mechanisms which theoretic considerations and the work of other investigators had led us to anticipate. Among other factors, we expected to find an accelerated rate of circulation, more efficient extraction of oxygen from the blood passing through the tissues and a greater cardiac output. In fact, we were unable to demonstrate significant alterations in circulatory rate except in a patient who showed a distinctly pathologic increase of arm to tongue time. We found too that the efficiency of the blood in supplying oxygen to the tissues was less than expected, for on the average the saturation of arterial blood with oxygen was less complete in the anemic children than in either the control subjects or the patients themselves after treatment of anemia. Moreover, while it was true that the tissues of the anemic subjects were able to extract a greater percentage of the available arterial oxygen, the quantitative exchange (arteriovenous oxygen difference) was markedly diminished.

These facts led us to conclude that an increased cardiac output must be the most important compensatory adjustment in anemia. Unfortunately no accurate means for estimating cardiac output was available to us, since all the methods in common use required greater cooperation than our subjects could give. The fact that during rest the pulse rates of the anemic children were more rapid than those of 9 of the 10 control subjects suggested that there might be an augmentation of the minute volume output. We attempted to confirm this impression roentgenographically by taking roentgenkymograms, from which we computed Johnson's roentgenkymographic index, but we were thwarted by the complex technic and by multiple inaccuracies in the manner of

calculation. Estimations of output based on figures for the arteriovenous oxygen difference (Fick principle) consistently indicated a greatly increased stroke volume, but the well recognized fallacies [20] associated with this system are not minimized, and may even be increased, by anemia. Consequently we hesitate to accept these results as proof, though we retain our conviction that an increase in cardiac output plays the primary role in the body's adaptation to anemia.

It is known from clinical observation that in severe anemia the heart eventually may be unable to stand the strain associated with the increased demand of the body for blood, so that failure with congestion may ensue. If the anemia is of only moderate severity or duration, less obvious changes in cardiac function may be expected. We shall now examine the evidence which we have collected in support of such dysfunction or limitation of reserve. Our subjects may be divided into two types, each of which will be discussed separately: 4 patients with chronic (erythroblastic and hypoplastic) anemia of three or more years' duration and 1 patient with acute anemia secondary to hemorrhage.

Evidence of Myocardial Dysfunction.—1. Patients with Chronic Anemia: The symptoms of which these patients complained did not as a rule suggest cardiac damage but seemed more directly related to the anemia. Shortness of breath, the predominant symptom of the failing myocardium, was conspicuously absent. Weakness and lassitude were more common complaints.

Clinical evidence of myocardial abnormality, however, was present on physical examination. Enlargement of the heart was suspected in all 4 cases and confirmed roentgenologically in 3. Tachycardia, alteration in the quality of the heart sounds and systolic murmurs were likewise found in all members of the group. Gallop rhythm was present in 2 instances. One child had signs of heart failure with venous engorgement, an enlarged liver and edema of the ankles, but these signs diminished remarkably after three days' rest in bed.

We do not attach much importance to measurements of vital capacity, since accurate estimations are difficult to obtain even for older and more intelligent children. It is perhaps significant that in spite of their freedom from dyspnea, all of our patients had vital capacities which were considerably less than normal.

Despite these evidences of myocardial involvement, all 4 members of the group were found to have a comparatively normal response to the exercise tolerance test (a comparison of pulse rate, respiratory rate and blood pressure during rest and two minutes after the completion

20. Altschule, M. D.: The Pathological Physiology of Chronic Cardiac Decompensation, Medicine **17**:75, 1938.

of a standard amount of exercise). This result was not totally unexpected, for we had observed that these children were handicapped little if at all in their ability to play and take exercise with other children. But although the simpler clinical tests of cardiac function failed to reveal striking evidence of abnormality, electrocardiographic and roentgenographic studies disclosed certain unusual changes following exercise.

We confirmed the observations of other workers that in normal children exercise produces an increase in the size of the electrocardiographic complexes, notably the T waves. At rest the anemic children showed no definitely abnormal electrocardiographic findings, but after exercise 3 of them exhibited a reduction in the size of the T waves, and in 1 case the RT segment was depressed below the isoelectric line. The latter change was of the type that has been demonstrated in anoxemia. As far as we know, such aberrations have not previously been demonstrated in the anemias of children.

Roentgenkymography, which permits reconstruction of the cardiac silhouette during any phase of the cardiac cycle, enabled us to adduce additional evidence of myocardial dysfunction. Our observations on the control children lent support to previous reports that the normal heart is smaller immediately after exercise than in the resting state. In the anemic subjects we found that occasionally the reverse was true. In addition, the roentgenkymograms of some of the anemic children showed rounded waves with narrow excursions, which were interpreted as an indication of poor myocardial tone.

In summary it may be said that chronic anemia fails to produce either the symptoms of cardiac damage or any significant alterations in the results of ordinary tests of cardiac function. On the other hand, measurements of vital capacity and electrocardiographic and roentgenographic determinations of the cardiac response may reveal abnormalities.

2. Patient with Acute Anemia: Circumstances made it impossible to study more than a single child with acute anemia severe enough to be comparable with the chronic types. It would therefore be unwise to conclude that our findings in this case are necessarily typical. Despite the complete absence of symptoms or physical signs pointing to myocardial insufficiency, this patient showed an obviously defective response to the exercise tolerance test. On the other hand, no abnormalities were seen in the electrocardiograms either before or after exercise, nor did the roentgenkymograms differ from those of the control subjects. Likewise vital capacity, circulatory rate, venous pressure and cardiac size were normal.

Common sense dictates that if damage to the heart is caused by anemia, it is more severe in the child whose anemia is of several years' standing than in the child who has been anemic for a few days only. The paradoxic results of the exercise tolerance test and their variance from results of other methods of estimating cardiac function have made us skeptical of its value and have led us to the conclusion, shared by other workers, that an unusual reaction to the test is not necessarily an indication of impaired cardiac function.

Evidence of Cardiac Recovery.—The onset of heart failure in chronic anemia is insidious, but once it is established a vicious circle results. The patient depends on an efficient cardiovascular system to compensate for his anemia, while the heart depends on properly oxygenated blood for the maintenance of its efficiency. The mere fact that this circle may be broken by treatment of the anemia (attested by clinical observation and previous reports) is strong evidence that the cardiac damage associated with the anemia is not completely irreparable. We shall now consider the additional evidence which we have gathered in support of this contention.

1. Patients with Chronic Anemia: Clinical evidence of improvement following transfusion was usually apparent from changes in the results of physical examination. The pulse rate became slower in each instance. The quality of the heart sounds improved, and murmurs diminished in intensity. A fall in systolic and a slight rise in diastolic blood pressure, leading to diminution in pulse pressure, was usual. In 3 of the 4 patients percussion and palpation of the apical impulse indicated diminution in cardiac size, but we found it difficult to confirm this impression by roentgen study. This was partly due to the stringency of our criteria, for we demanded that the decrease should be visible in two projections and that the films should conform to certain recognized standards for comparison. In 2 cases one projection showed a considerable reduction in size after treatment, but in neither instance was a similar decrease visible in films exposed from another angle. We have therefore been unable to demonstrate objectively that the heart which has become enlarged as a result of chronic anemia will shrink in response to therapy. Further, we believe that descriptions of minor changes of cardiac size in children when based on roentgen evidence should be accepted with great caution. The technical difficulties are at present too numerous to allow clearcut results.

Although most of these patients showed slight improvement in response to exercise as judged by the behavior of pulse, respirations and blood pressure, little significance can be attached to the results of the test for reasons which have been advanced. Minor improvement in the form of the electrocardiograms taken during rest was reflected

by a slight shortening of the PR interval. All 3 children who showed an abnormal electrocardiographic response to exercise before treatment had much more normal tracings after their hemoglobin concentrations had been raised. In the case of the child who had shown depression of the RT segment this improvement was especially striking and was maintained even after strenuous exertion. In like manner, after transfusion, roentgenkymographic films taken after exercise showed a more consistently normal response, and an improvement in the form of the kymographic waves suggested an increase in myocardial tone.

Abnormal values for venous pressure and circulation time were found in a patient who presented other evidence of congestive heart failure at the time of admission. Both readings returned to the normal range after transfusion.

The effect of treatment on cardiac output had to be determined by the Fick principle. Altschule [20] recently pointed out the inherent weaknesses of this method, and we have stressed our unwillingness to accept conclusions based on this form of calculation. However, it is interesting to notice that transfusion apparently raised the already increased minute volume output of 3 of the 4 patients. The fourth patient showed a moderate decrease. Such findings, although paradoxic, may be related to the vicious circle previously referred to in this paper. At some point anemia may so seriously hamper the efficiency of the myocardium that it is unable to produce an optimal output. Transfusion might then reasonably be expected to increase rather than decrease the amount of blood pumped.

Thus from a study of several different aspects of cardiac function we conclude that treatment of anemia in these patients was followed by considerable recovery from functional impairment of the heart, although morphologic recovery was not complete.

2. Patient with Acute Anemia: Our only evidence of abnormal cardiac function before transfusion was the response to the exercise tolerance test. This was not significantly altered by treatment.

Summary.—A study of various aspects of cardiac function in 5 anemic children, of whom 4 had been anemic for three or more years, led to the following conclusions:

1. The function of the heart is adversely affected by anemia. Changes are maximal in anemia of long duration and minimal in moderate anemia of short duration.

2. An increase of cardiac output is the most important compensatory mechanism in the anemic patient.

3. Simple indications of cardiac reserve, such as the response of pulse, respirations and blood pressure to a given amount of exercise,

may be highly misleading in the estimation of degrees of cardiac embarrassment.

4. Treatment of anemia leads to improvement in cardiac function, the amount of recovery being inversely related to the duration of the anemia.

There is at present a tendency to allow children suffering from erythroblastic or sickle cell anemia to live with relatively low concentrations of hemoglobin, since in such circumstances they require fewer transfusions and often manufacture sufficient red cells to maintain constant blood counts. This practice is condoned because such patients are apparently but slightly incapacitated by their anemia and exhibit little shortness of breath or reduction in their capacity for exercise. Yet when the heart is examined carefully the majority of these children show signs of cardiac involvement. Gross limitation of activity may not appear until late childhood, when frank heart failure occurs and it is probably too late for really effective treatment. Once severe cardiac damage has taken place it is only partially remediable, and in addition active treatment may encompass dangers which are not present for children with properly functioning circulatory systems. The latter point is well illustrated in a case in our series in which an attempt to increase the hemoglobin to a normal level was followed by a cerebral accident. Despite the fact that the transfusions were given slowly and in small amounts over five days and despite clinical evidence of great improvement in the circulatory system, there suddenly developed signs of intracranial pressure followed by coma and convulsions. Following strenuous treatment the condition of this patient gradually improved, but hemiplegia developed, which was fortunately temporary. We interpreted the episode as due to thrombosis of a cerebral vessel. Another accident, perhaps more directly attributable to myocardial weakness, occurred at the Babies Hospital in a child with severe erythroblastic anemia, when transfusion of a small amount of blood led to pulmonary edema and a fatal termination.

We believe that if the hemoglobin level could be kept high from the time that anemia is first discovered, changes in the heart muscle might be prevented, or at any rate greatly retarded, and that certain of the accidents associated with transfusion might be avoided.

Dr. Rustin McIntosh gave suggestions and criticism.

MENINGITIS CAUSED BY PNEUMOCOCCUS TYPE III

OBSERVATIONS ON SULFANILAMIDE THERAPY

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A new type of therapeutic agent effective against certain virulent bacterial infections was elaborated after many years of pioneer work on the chemical properties of azo dyes.[1] Domagk[2] in 1935 reported on the use of the original prontosil in the treatment of experimental streptococcic infections in mice. He found that a sulfonamide group in certain azo dyes caused them to protect or cure mice infected with fatal doses of hemolytic streptococci. The most effective of these dyes are 4-sulfamido-2′-4′-diaminoazobenzene hydrochloride (the original prontosil) and the disodium salt of 4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3′, 6′-disulfonic acid (the compound known as prontosil soluble and then as prontosil and now to be called neoprontosil). A short time later the Tréfouëls, Nitti, Bovet and Fourneau[3] noted that paraaminobenzenesulfonamide constitutes the

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1. Gelmo, P.: Ueber Sulfamide der p-Amidobenzolsulfonsäure, J. f. prakt. Chem. **77**:369-382 (April 3) 1908; Chem. Abstr. **2**:2551 (Sept.) 1908. Hoerlein, H.: New Class of Chemotherapeutic Agents Against Streptococci, with Special Reference to Prontosil and Prontylin, M. Rec. **146**:11-13 (July 7) 1937. Sisley, P., and Porcher, C.: Du sort des matières colorantes dans l'organisme animal, Compt. rend. Acad. d. sc. **152**:1062-1064, 1911. Eisenberg, P.: A Study of the Specificity of Disinfectants: The Action of Dyes on Bactereia and the Effect of Vital Staining on the Growth of Bacteria, Chem. Abstr. **8**:3063-3064. 1914. Collins, G. W.: Chemical Examination of Pyridium and Mallophene, J. Am. Pharm. A. **20**:455-462 (May) 1931. Jacobs, W. A., and Heidelberger, M.: On Amides, Uramino Compounds, and Ureides Containing an Aromatic Nucleus, J. Am. Chem. Soc. **39**:2418-2443 (Nov.) 1917.

2. Domagk, G.: Ein Beitrag zur Chemotherapie der bakteriellen Infektionen, Deutsche med. Wchnschr. **61**:250-253 (Feb. 15) 1935.

3. Tréfouël, J.; Tréfouël, J. (Mme.); Nitti, F., and Bovet, D.: Activité du p-aminophénylsulfamide sur les infections streptococciques expérimentales de la souris et du lapin, Compt. rend. Soc. de biol. **120**:756-758, 1935. Nitti, F., and Bovet, D.: Action du 4-sulfonamide-2-4 diamino-benzol (prontosil) sur des

active fraction of both the prontosils; they then synthesized paraaminobenzenesulfonamide, later to be known as sulfanilamide. Their observations were confirmed and elaborated by Goissedet, Despois, Gailliot and Mayer [4] and Levaditi and Vaisman [5] in France and by Buttle, Gray and Stephenson [6] and Colebrook and Kenny [7] in England. It was soon demonstrated that the prontosils can be reduced in vitro, with the formation of paraaminobenzenesulfonamide.[8] In experiments reported in 1937 Long and Bliss [9] used cysteine to reduce prontosil in experiments with cultures of streptococci and found that the resulting product was bacteriostatic. Marshall, Cutting and Emerson [10] observed that sulfanilamide is excreted in the urine of both animals and human beings

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infections streptococciques de la souris provoquées par des streptocoques d'origine humaine, ibid. **119**:1277-1280, 1935. Fourneau, E.; Tréfouël, J.; Tréfouël, J. (Mme.); Nitti, F., and Bovet, D.: Chimiothérapie des infections streptococcique par les dérives du aminophénylsulfamide, ibid. **122**:285-259, 1936; Action du paraaminophénylsulfamide sur les moisissures, ibid. **122**:652-654, 1936.

4. Goissedet, P.; Despois, R.; Gailliot, P., and Mayer, R.: De l'action du radical sulfamide: SO^2NH^2 sur l'infection streptococcique expérimentale de la souris, Compt. rend. Soc. de biol. **121**:1082-1084, 1936.

5. Levaditi, C., and Vaisman, A.: Mécanisme de l'action curative et préventive du chlorhydrate de 4'sulfamido-2.-4. diaminoazobenzène et d'autres dérivés similaires dans l'infection streptococcique expérimentale, Compt. rend. Soc. de biol. **120**:1077-1079, 1935.

6. Buttle, G. A. H.; Gray, W. H., and Stephenson, D.: Protection of Mice Against Streptococcal and Other Infections by *p*-Aminobenzenesulfonamide and Related Substances, Lancet **1**:1286-1290 (June 6) 1936.

7. Colebrook, L., and Kenny, M.: Treatment of Human Puerperal Infections and of Experimental Infections in Mice with Prontosil, Lancet **1**:1279-1286 (June 6) 1936.

8. Colebrook, L.; Buttle, G. A. H., and O'Meara, R. A. Q.: Mode of Action of *p*-Aminobenzenesulfonamide and Prontosil in Hemolytic Streptococcal Infections, Lancet **2**:1323-1326 (Dec. 5) 1936.

9. Long, P. H., and Bliss, E. A.: Treatment of Certain Infections with Sulfanilamide or Its Derivatives, Internat. S. Digest **23**:259-265 (May) 1937; Para-Aminobenzenesulfonamide and Its Derivatives: Experimental and Clinical Observations on Their Use in the Treatment of Beta-Hemolytic Streptococcic Infections, J. A. M. A. **108**:32-37 (Jan. 2) 1937; Use of Para-Aminobenzenesulfonamide or Its Derivatives in the Treatment of Infections Due to Beta-Hemolytic Streptococci, Pneumococci and Meningococci, South. M. J. **30**:479-487 (May) 1937; Activation of "Prontosil Solution" in Vitro by Reduction with Cysteine Hydrochloride, Bull. Johns Hopkins Hosp. **60**:149-153 (Feb.) 1937. Bliss, E. A., and Long, P. H.: Observations on the Mode of Action of Sulfanilamide, J. A. M. A. **109**:1524-1528 (Nov. 6) 1937.

10. Marshall, E. K., Jr.; Cutting, W. C., and Emerson, K., Jr.: Acetylation of Para-Aminobenzenesulfonamide in the Animal Organism, Science **85**:202-203 (Feb. 19) 1937; Para-Aminobenzenesulfonamide: Absorption and Excretion Method of Determination in Urine and Blood, J. A. M. A. **108**:953-957 (March 20) 1937.

and devised a method of determining the concentration of the drug in the blood, which has been valuable in the administration of optimum doses of sulfanilamide.

Domagk [2] originally claimed some effect of prontosil against the type III pneumococcus, and Rosenthal and his co-workers [11] obtained consistent chemotherapeutic activity against pneumococci of types I, II and III in experimentally induced infections. In all cases there was marked prolongation of the life of the animals, and a considerable percentage of the animals with the strains most favorably affected survived permanently. In the instance of type III pneumococci, favorable results have also been reported by Cooper, Gross and Mellon.[12] The action of sulfanilamide in combating type III pneumococcic infection in mice does not appear at first to be as effective as its action in either streptococcic or meningococcic infection. However, when the extreme susceptibility of mice to pneumococci is considered, the degree of protection demonstrated possibly assumes greater magnitude, even though the number of fatal doses against which protection was obtained was not so high as with streptococcic or meningococcic infection. Branham and Rosenthal [13] reported on combined sulfanilamide and serum therapy for pneumococcic infections in mice and suggested that drug therapy be used as an adjunct to serum treatment or when serum is ineffective or not available.

These experimental results prompted us to employ sulfanilamide in the treatment of a patient with meningitis due to Pneumococcus type III. This patient was hospitalized and treatment instituted three days after the onset of symptoms. The prolonged course enabled us to obtain valuable clinical and laboratory data with reference to sulfanilamide therapy.

REPORT OF A CASE

M. H., an 11 year old boy, was admitted to the Jewish Hospital on Oct. 20, 1937, because of headache, fever and slight nuchal rigidity of about three days' duration. On admission he appeared well developed and well nourished. The temperature was 104 F., the pulse rate was 124, and the respiratory rate was 24

11. Rosenthal, S. M.: Chemotherapy of Experimental Pneumococcus Infections, Pub. Health Rep. **52**:48-53 (Jan. 8) 1937; The Effect of *p*-Aminobenzenesulfonamide on Pneumococci in Vitro, ibid. **52**:192-196 (Feb. 12) 1937. Rosenthal, S. M.; Bauer, H., and Branham, S. E.: Comparative Studies of Sulfanilamide Compounds in Experimental Pneumococcus, Streptococcus and Meningococcus Infections, ibid. **52**:662-671 (May 21) 1937.

12. Cooper, F. B.; Gross, P., and Mellon, R. R.: The Action of *p*-Aminobenzenesulfonamide on Type III Pneumococcus Infections in Mice, Proc. Soc. Exper. Biol. & Med. **36**:148-151 (March) 1937.

13. Branham, S. E., and Rosenthal, S. M.: Sulfonilamide, Serum, and Combined Serum and Drug Therapy in Experimental Meningococcus and Pneumococcus Infections in Mice, Pub. Health Rep. **52**:685-695 (May 28) 1937.

per minute. The head was normal. The eyes reacted to light and in accommodation; the pupils were equal and regular; the extraocular movements were normal. A lag of the left lid and left external rectus palsy had been present since birth. The fundi revealed no pathologic change. The ears were normal. There was no nasal discharge. The tongue was coated and moist; the pharynx was granular and red; the posterior pharyngeal wall was covered with thick purulent discharge. The posterior cervical lymph nodes were moderately enlarged. There was some resistance to anterior flexion of the neck. The chest was clear, and the heart showed no abnormalities. The abdomen was soft; the liver and spleen were not palpable. Neurologic examination revealed active deep reflexes, Babinski's sign on the left and absence of Kernig's sign. There were no other abnormalities of the cranial nerves, and no motor or sensory disturbances. The clinical impression was "meningitis."

The laboratory data and therapy are presented in the table.

Laboratory Data and Therapy

Days in Hospital	Dose of Sulfanilamide, Grains		Concentration of Sulfanilamide, Mg. per 100 Cc.		Spinal Fluid, Cell Count
	Oral	Intrathecal	Blood	Spinal Fluid	
1	60	..	11.9	5.9	4,750
4	75	20	6.2	4.8	12,500
6	75	20	8.9	7.5	3,600
9	75	20	7.5	6.6	5,050
11	75	..	...	6.0	2,100
13	50	..	4.0	4.4	3,050
16	50	40	...	4.2	2,975
17	50	40	5.7	3.7	1,000
18	50	12	...	3.2	2,585
19	75	40	...	3.6	3,575
20	75	..	...	5.0	3,770
23	65	40	...	5.1	1,825
25	75	..	...	4.7	2,225
26	75	..	...	4.5	7,025
28	75	..	...	6.7	8,850
29	75	..	...	6.8	2,400
30	75	..	...	7.0	1,380
31	75	..	...	4.4	1,200
32	75	..	...	5.2	800
33	15	..	3.5	4.0	1,400

Treatment and Course.—The patient was given 60 grains (3.6 Gm.) of sulfanilamide by mouth within the first twenty-four hours and 75 grains (4.5 Gm.) daily thereafter. This dosage was continued for twelve days, after which a marked drop of the hemoglobin level and red cell count forced a reduction of the dose to 50 grains (3 Gm.). When the hemoglobin content and red cell count dropped below 50 per cent and 3,000,000, respectively, frequent transfusions became necessary.

On admission, a lumbar tap yielded cloudy gray fluid under increased pressure. The cell count was 5,000 per cubic millimeter, with 40 per cent polymorphonuclear leukocytes and 60 per cent lymphocytes. The qualitative sugar test showed a moderate diminution of reducing substance. A smear (Gram's stain) showed no organisms. Lumbar taps were performed twice daily, and with each, 15 cc. of antimeningococcus serum was injected intrathecally until two days after admission, when the spinal fluid culture showed Pneumococcus type III. From then on the patient received intrathecally 20 to 40 cc. of an 0.8 per cent solution of sulfanilamide in a physiologic solution of sodium chloride in place of the serum. On the twenty-fifth day lumbar block occurred, and daily cisternal taps were performed.

Lederle's type III pneumococcus serum was injected intrathecally for a few days, but its use was discontinued when the lumbar block occurred. Our experience with this serum has not been sufficient to permit any conclusions.

The concentration of sulfanilamide in the blood and in the spinal fluid was determined according to the method of Marshall, Emerson and Cutting.[10]

On October 22, two days after admission, the patient began to manifest euphoria. Examination showed marked nuchal rigidity, bilateral presence of Kernig's sign, absence of knee jerks, haziness of the margins of the optic disks, an irregular hemorrhagic area on the nasal side of the left disk, and marked engorgement of the retinal vessels.

On October 24 the patient became irrational and was deeply cyanotic. The hemoglobin percentage was 86 and the red cell count 4,260,000. Administration of sulfanilamide was continued despite the cyanosis. Marked nuchal rigidity persisted, and opisthotonos was noted; the superficial reflexes were diminished. The hemorrhagic area within the left fundus was larger, and the disk margins were more indistinct.

From October 25 to November 2 the patient appeared to improve; he was better oriented and less irrational, and the nuchal rigidity was diminished. The hemorrhage within the left fundus was being absorbed. The activity of the reflexes varied daily. Roentgenograms of the skull and sinuses showed no pathologic changes.

On November 7 the patient's general condition became poor; nuchal rigidity was more marked, and Kernig's and Brudzinski's signs were elicited bilaterally.

On November 8, despite negative roentgen findings, the sinuses were explored and cultures made of the washings. The cultures yielded no pneumococci.

On November 13 the head was markedly retracted. The abdomen was rigid and tender. Pneumococcic peritonitis was considered. The blood culture was repeatedly sterile.

On November 15 the patient was disoriented; there were tremors of both upper extremities associated with picking at the bed clothes. Cisternal taps became necessary because of lumbar block.

On November 17 the patient's condition became worse, and there was marked opisthotonos. The fundi showed no further changes. There was right internal strabismus. The patient's restlessness required unusually large doses of sedatives, including morphine sulfate and paraldehyde.

On November 21 the patient was disoriented, cyanotic and dyspneic. The extremities were cold and clammy. There was nystagmus of both eyes. Many coarse and fine moist rales were heard throughout the chest.

On November 23 urinary incontinence developed. The pupils were dilated and responded sluggishly to light. The heart tones were poor in quality, and the liver extended 3 cm. below the costal margin.

On November 24 the patient died. Permission for necropsy was refused.

COMMENT

The mode of action of sulfanilamide is still subject to discussion. Domagk [2] noted that phagocytosis played an important role in experimental streptococcic infections in mice. Colebrook and Kenny [7] observed that serums of normal human beings and those of certain laboratory animals which had received parenteral injections of sulfanilamide did not have an inhibitory effect on streptococci in vitro. However, serums

from patients ill with streptococcic infections did have a definite bacteriostatic effect in vitro after treatment with the prontosils. Long and Bliss [9] concluded from their observations that bacteriostasis played a role in the control of streptococcic infections in mice. The demonstration of unchanged sulfanilamide in the urine of patients treated with this drug strongly suggested that the action was due to sulfanilamide itself and not to some derivative.[14] Gay and Clark [15] in their work on experimental streptococcic empyema concluded that sulfanilamide produced bacteriostasis sufficiently marked to protect the accumulated leukocytes and to allow the natural defense macrophages to be effective but that it did not stimulate the mobilization of macrophages. Bigler, Clifton and Werner [16] administered sulfanilamide at the rate of 1 Gm. per 20 pounds (9.1 Kg.) and stated that the effective action was independent of the leukocytes since neither their total number nor the proportion of polymorphonuclear leukocytes was increased. Recently Osgood and Brownlee [17] employed cultures of bone marrow in their investigations and observed that the major action of sulfanilamide on streptococci of the beta hemolytic type seemed to be that of a neutralization of the toxins and a depression of the rate of cell division of the organisms. They concluded that sulfanilamide had no direct effect on phagocytosis.

It has been suggested [9] that for patients weighing 100 pounds (45.4 Kg.) and over the dosage of sulfanilamide is 50 to 80 grains (3 to 4.8 Gm.) for the initial dose and 15 grains (0.9 Gm.) every four hours. Our patient, who weighed 100 pounds on admission, received 30 grains (1.8 Gm.) immediately and thereafter 15 grains every four hours, five times daily. Within twelve hours the concentration of sulfanilamide was 11.9 mg. per hundred cubic centimeters in the blood and 5.9 mg. in the spinal fluid. In addition to the oral doses of the drug the patient received intrathecally 20 to 40 cc. of an 0.8 per cent solution of sulfanilamide in a physiologic solution of sodium chloride. The variations in the concentration of the drug in the blood and spinal fluid are noted in the table. It is interesting to observe that on October 28 the intrathecal administration of sulfanilamide was temporarily discontinued and the oral dose was reduced to 50 grains daily

14. Fuller, A. T.: Is *p*-Aminobenzenesulphonamide the Active Agent in Prontosil Therapy? Lancet **1**:194-198 (Jan. 23) 1937. Marshall, Cutting and Emerson.[10]

15. Gay, F. P., and Clark, A. R.: On the Mode of Action of Sulfanilamide in Experimental Streptococcus Empyema, J. Exper. Med. **66**:535-548 (Nov.) 1937.

16. Bigler, J. A.; Clifton, W. M., and Werner, M.: The Leukocyte Response to Sulfanilamide Therapy, J. A. M. A. **110**:343-349 (Jan. 29) 1938.

17. Osgood, E. E., and Brownlee, I. E.: Studies on the Mode of Action of Sulfanilamide, J. A. M. A. **110**:349-356 (Jan. 29) 1938.

because of the development of marked anemia. Nevertheless, two days later the concentration in the spinal fluid was 6 mg. per hundred cubic centimeters. Again, because of lumbar block, sulfanilamide was administered only by mouth, and the concentration in the spinal fluid varied from 4.4 to 7 mg. These observations lead us to question the efficacy or necessity of intrathecal administration provided adequate oral intake is maintained, as determined by the concentrations of sulfanilamide. They also emphasize the ease with which the drug diffuses into the spinal fluid.

The literature has recently been replete with reports of toxic effects of small or large doses of sulfanilamide. Some of these effects were probably the result of an idiosyncrasy to even small doses; others, of toxicity from accumulated doses.[9] Among the effects reported have been fever, dizziness, nausea, anorexia, cyanosis, acidosis, sulfhemoglobinemia and methemoglobinemia, cutaneous rashes, granulopenia and hemolytic anemia.[18] Some of these effects were noted in our patient, but not all of them were indications for the discontinuation of sulfanilamide. For instance, two days after therapy had begun deep cyanosis developed, yet there was no influence on the blood picture. The administration of sulfanilamide was therefore continued. Furthermore, tests for sulfhemoglobin and methemoglobin were negative. However, on October 28 the hemoglobin percentage fell to 54 and the red cell count to 2,800,000. The daily oral dose of sulfanilamide was reduced to 50 grains, and no sulfanilamide was given intrathecally. Despite frequent transfusions, the hemoglobin content and the red cell count remained somewhat depressed. Transient leukopenia together with a shift to the left in the Schilling differential count occurred soon after the effect on the red cells and on the hemoglobin was noted. A study of the sternal bone marrow revealed a marked shift to the left and

18. Southworth, H.: Acidosis Associated with the Administration of Prontylin, Proc. Soc. Exper. Biol. & Med. **36**:58-61 (Feb.) 1937. Hageman, P. O., and Blake, F. G.: A Specific Febrile Reaction to Sulfanilamide, J. A. M. A. **109**:642-646 (Aug. 28) 1937. Marshall, E. K., Jr.; Cutting, W. C., and Emerson, K., Jr.: The Toxicity of Sulfanilamide, ibid. **110**:252-257 (Jan. 22) 1937. Menville, J. H., and Archmard, J. J.: Skin Eruptions in Patients Receiving Sulfanilamide, ibid. **109**:1008-1009 (Sept. 25) 1937. Borst, J. G. G.: Death from Agranulocytosis After Treatment with Prontosil Flavum, Lancet **1**:1519-1520 (June 26) 1937. Young, C. J.: Agranulocytosis and Para-Amino-Benzene Sulphonamide, Brit. M. J. **2**:105-106 (July 17) 1937. Harvey, A. M., and Janeway, C. A.: Development of Acute Hemolytic Anemia During the Administration of Sulfanilamide (Para-Aminobenzenesulfonamide), J. A. M. A. **109**:12-16 (July 3) 1937. Paton, J. P. T., and Caton, J. C.: Sulfhemoglobinemia and Methemoglobinemia Following the Administration of *p*-Aminobenzenesulfonamide, Lancet **1**:1159-1162 (May 15) 1937.

increase in the activity of the erythropoietic function. It was concluded from this study that the marrow represented a compensatory reaction of both myeloid and erythrogenic components.

On October 24, four days after admission, the spinal fluid culture became sterile. There had been a total intake of 285 grains (17.1 Gm.) of sulfanilamide given orally and 22 cc. of an 0.8 per cent solution of sulfanilamide given intrathecally. From that time until November 2 the patient seemed to improve clinically. During this interval only 3 cultures of the spinal fluid were positive, and in these few colonies were noted. There was no significant reduction in the cell count, and the results of qualitative sugar tests were not consistent. Thereafter, however, the patient's condition continued to become worse, and cultures of the spinal fluid increasingly showed more colonies.

SUMMARY AND CONCLUSIONS

A case of meningitis caused by Pneumococcus type III is presented in which treatment was by oral and intrathecal administration of sulfanilamide.

An adequate concentration of the drug in the spinal fluid was maintained by oral administration alone—a fact which leads us to question the necessity of intrathecal administration.

Cyanosis in the course of treatment is no contraindication to the use of the drug, provided no abnormal alterations occur in the peripheral blood.

The temporary improvement under this form of therapy together with the definite prolongation of the life of the patient seems to encourage further attempts with this form of therapy in cases of meningitis due to Pneumococcus type III.

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TOTAL, DIFFERENTIAL AND ABSOLUTE LEUKOCYTE COUNTS AND SEDIMENTATION RATES FOR HEALTHY CHILDREN

STANDARDS FOR CHILDREN EIGHT TO FOURTEEN YEARS OF AGE

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It is the purpose of this article to supply more accurate data than have heretofore been available on total, differential and absolute leukocyte counts and on sedimentation rates for healthy children 8 to 14 years of age. This is one of a series of papers on hematologic standards for healthy persons from birth through adult life. The data for other age groups have been or will be reported elsewhere.[1]

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1. (*a*) Osgood, E. E.: Hemoglobin, Color Index, Saturation Index, and Volume Index Standards, Arch. Int. Med. **37**:685 (May) 1926. (*b*) Osgood, E. E., and Haskins, H. D.: The Relation Between Cell Count, Cell Volume, and Hemoglobin Content of the Venous Blood of Normal Young Women, ibid. **39**: 643 (May) 1927. (*c*) Osgood, E. E., and Baker, R. L.: Erythrocyte, Hemoglobin, Cell Volume and Color, Volume and Saturation Index Standards for Normal Children of School Age, Am. J. Dis. Child. **50**:343 (Aug.) 1935. (*d*) Osgood, E. E.: Normal Hematologic Standards, Arch. Int. Med. **56**:849 (Nov.) 1935. (*e*) Osgood, E. E.; Baker, R. L.; Brownlee, I. E.; Osgood, M. W.; Ellis, D. M., and Cohen, W.: Total, Differential and Absolute Leukocyte Counts and Sedimentation Rates of Healthy Children Four to Seven Years of Age, Am. J. Dis. Child. **58**:61 (July) 1939. (*f*) Osgood, E. E., and others: Total, Differential and Absolute Leukocyte Counts and Sedimentation Rates Determined for Healthy Adolescents Fifteen to Eighteen Years of Age, J. Lab. & Clin. Med., to be published. (*g*) Osgood, E. E.; Brownlee, I. E.; Osgood, M. W.; Ellis, D. M., and Cohen, W.: Total, Differential and Absolute Leukocyte Counts and Sedimentation Rates for Healthy Persons Nineteen Years of Age and Over, Arch. Int. Med. **64**: 105 (July) 1939. (*h*) Chuinard, E. G.; Osgood, E. E., and Ellis, D. M.: Total, Differential and Absolute Leukocyte Counts and Sedimentation Rates for Healthy

(Footnote continued on next page)

Examination of the literature reveals that there are almost no studies by modern methods of the total, differential and absolute leukocyte counts for strictly healthy American children in the age group under consideration. Such figures as are available have been based almost entirely on studies of sick children, although these children were thought by the investigators to have illnesses not likely to affect the leukocyte count.[2] Carstanjen,[3] Karniski [4] and Perlin [5] reported results of studies made in Europe prior to 1903. Keller [6] studied total leukocyte counts on 500 children in connection with a survey of hookworm disease. Kato [7] reported the average leukocyte counts of children "with non-hematologic conditions." The figures given in the textbooks of pediatrics [8] seem to have been based on these few unsatisfactory studies, modified by the authors' clinical impressions of the normal leukocyte count.

SUBJECTS

All the children lived in or near Portland, Ore., at an elevation of less than 500 feet (152.4 meters). All were white and native born and in most instances were children of native-born parents. They were from

Newborn Infants, to be published. (*i*) Chuinard, E. G.; Osgood, E. E., and Ellis, D. M.: Erythrocyte Counts, Hemoglobin, Cell Volume, and Color, Volume and Saturation Index Standards for Healthy Newborn Infants, to be published. (*j*) Osgood, E. E., and others: Erythrocyte Counts, Hemoglobin, Cell Volume, and Color, Volume and Saturation Index Standards for Healthy Adolescent Males, Fifteen Years of Age and Over, to be published; (*k*) Erythrocyte Counts, Hemoglobin, Cell Volume, and Color, Volume and Saturation Index Standards for Healthy Females, Fifteen Years of Age and Over, to be published; (*l*) Reticulocyte Counts in Healthy Newborn Infants, to be published; (*m*) Icterus Index Determinations in Healthy Newborn Infants, to be published; (*n*) Reticulocyte Counts in Healthy Adolescent Boys and Girls, to be published.

2. Unless the counts of a large series of subjects having a certain disease have been compared with the counts of a statistically significant series of healthy persons of the same age group, it is unjustifiable to assume that that disease does not alter the leukocyte count.

3. Carstanjen, M.: Wie verhalten sich die procentischen Verhältnisse der verschiedenen Formen der weissen Blutkörperchen beim Menschen unter normalen Umstanden? Jahrb. f. Kinderh. **2**:215, 333 and 684, 1900.

4. Karniski, A. O.: Ueber das Blut gesunder Kinder, Arch. f. Kinderh. **36**: 42, 1903.

5. Perlin, A.: Beitrag zur Kenntnis der physiologischen Grenzen des Hämoglobingehalts und der Zahl der Blutkörperchen im Kindesalter, Jahrb. f. Kinderh. **58**:549, 1903.

6. Keller, A. E.: Unpublished data; cited by Garrey, W. E., and Bryan, W. R.: Variations in White Blood Cell Counts, Physiol. Rev. **15**:597, 1935.

7. Kato, K.: Leucocytes in Infancy and Childhood, J. Pediat. **7**:7, 1935.

8. Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1923, vol. 4, pp. 409 and 426. Griffith, J. P. C., and Mitchell, A. G.: Diseases of Infants and Children, ibid., 1937, pp. 37-39. Holt, L. E., and Howland, J.: Diseases of Infancy and Childhood, ed. 10, New York, D. Appleton-Century Company, Inc., 1936, p. 529.

the public schools, the orphanages, physicians' families and the outpatient clinic of the University of Oregon Medical School. Those from the clinic had been brought in for tonsillectomy but were found by the examining physician to have no indication for this operation. Children 8 to 14 years of age were grouped together because the scatter diagrams [1d] of values for these children showed no significant differences for the two sexes and no great variation with age within this range. Younger children [1e] have higher leukocyte counts but similar differential counts. Adolescents 15 to 18 years of age[1f] have similar leukocyte counts but different differential counts.

METHODS

Since the methods used have been described in detail elsewhere [9] they will be commented on only briefly here. Venous blood mixed with 2 mg. of dry potassium oxalate per cubic centimeter was used for all determinations and is recommended because it is more convenient to use and gives more accurate results than blood from the finger or ear. No difficulty was encountered in obtaining venous blood. The blood was taken at any time of day as in ordinary office practice.

The leukocyte counts were made with apparatus certified by the Bureau of Standards of the United States Department of Commerce. An area of 4 sq. mm. was counted on each of two dilutions, and all the precautions outlined by Osgood [9] were used. The differential cell counts were made on Wright's stained smears on glass slides. Buffer phosphate was used as a diluent. The details of smearing and staining are described elsewhere.[10] In making the differential counts we classified 200 or more cells according to the criteria described and illustrated in the "Atlas of Hematology," [11] taking care to study only such portions of the smears as were thin enough that the akaryocytes (erythrocytes) were not touching each other. The absolute leukocyte counts were calculated by multiplying the total leukocyte count by the percentage of the particular cell type. Plum [12] has given data from which the probable error of any of these determinations may be calculated.

The sedimentation rates we determined on the same samples of oxalated blood, using a Westergren pipet and taking readings after fifteen and after forty-five minutes. Experience with over 80,000 determinations by this method has shown it to have the advantages of the graphic methods and to be simpler and quicker.

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TABLE 1.—*Total, Differential and Absolute Leukocyte Counts and Sedimentation Rates for Children Eight Years Old* *

Leukocytes per Cu. Mm.†	Neutrophil Lobocytes‡		Neutrophil Rhabdocytes§		Eosinophil Lobocytes		Basophil Lobocytes		Lymphocytes		Monocytes		Disintegrated Cells		Sedimentation Rate	
	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	Mm. in 15 Min.	Mm. in 45 Min.
								Boys								
5.4	34	1.8	4	0.22	6	0.32	0	0.00	48	2.6	3	0.16	4	0.22	1.5	12.0
5.8	39	2.3	4	0.23	1	0.06	0	0.00	46	2.7	2	0.12	8	0.46	1.0	4.5
5.8	38	2.2	2	0.12	2	0.12	1	0.06	44	2.6	6	0.35	7	0.41	0.5	3.5
6.2	42	2.6	2	0.08	2	0.08	0	0.00	46	2.9	2	0.08	6	0.37	1.5	10.0
6.2	29	1.8	1	0.06	2	0.12	0	0.00	64	4.0	2	0.12	2	0.12	1.5	5.5
6.4	28	1.8	6	0.38	4	0.26	1	0.06	51	3.3	4	0.26	6	0.38	3.0	5.0
7.0	32	2.2	6	0.42	5	0.35	1	0.07	38	2.7	10	0.70	8	0.56	1.0	6 0
7.2	10	0.7	1	0.07	4	0.29	0	0.00	71	5.1	2	0.14	12	0.86	11.0	59 0
7.3	26	1.9	2	0.15	2	0.15	1	0.07	57	4.2	1	0.07	11	0.80	1.0	6.0
8.7	36	3.1	1	0.09	0	0.00	1	0.09	60	5.2	1	0.09	1	0.09	1.5	7.0
9.6	20	1.9	1	0.10	1	0.10	1	0.10	70	6.7	4	0.38	3	0.29	2.0	5.0
9.6	39	3.7	4	0.38	3	0.29	1	0.10	51	4.9	1	0.10	1	0.10	1.0	4.0
10.0	50	5.0	6	0.60	10	1.00	2	0.20	18	1.8	9	0.90	4	0.40	2.0	12.0
10.3	38	3.9	1	0.10	1	0.10	1	0.10	55	5.7	2	0.21	2	0.21	1.5	11.0
10.6	43	4.6	1	0.11	10	1.10	1	0.11	38	4.0	5	0.53	2	0.21	1.5	6.5
10.9	35	3.8	2	0.22	6	0.65	1	0.11	46	5.0	1	0.11	9	0.98	0.5	4.0
7.9	33.7	2.71	2.8	0.21	3.7	0.31	0.8	0.07	50.2	3.96	3.4	0.27	5.4	0.40	2.0	10.1
10.9	50	5.0	6	0.60	10	1.10	2	0.20	71	6.7	10	0.90	12	0.98	11.0	59.0
5.4	10	0.7	1	0.06	0	0.00	0	0.00	18	1.8	1	0.07	1	0.09	0.5	3.5
								Girls								
5.8	34	2.0	1	0.06	10	0.58	0	0.00	47	2.7	2	0.12	6	0.35	3.0	12.0
6.8	28	1.9	2	0.14	2	0.14	0	0.00	56	3.8	3	0.20	8	0.54	1.0	5.0
7.2	44	3.2	0	0.00	1	0.07	1	0.07	46	3.3	3	0.22	4	0.29	1.0	5.0
7.7	34	2.6	1	0.08	1	0.08	0	0.00	59	4.5	5	0.38	0	0.00	2.5	7.0
8.9	34	3.0	1	0.09	1	0.09	0	0.00	59	5.3	1	0.09	4	0.36	2.5	5.5
8.9	26	2.3	1	0.09	3	0.27	0	0.00	61	5.4	3	0.27	6	0.53	1.0	12.0
9.2	42	3.9	0	0.00	4	0.37	1	0.09	51	4.7	2	0.18	0	0.00	2.0	6 5
9.2	36	3.3	1	0.09	6	0.55	2	0.18	47	4.3	4	0.37	4	0.37	Q. N. S.	Q. N. S.
9.5	41	3.9	0	0.00	0	0.00	0	0.00	55	5.2	4	0.38	0	0.00	2.0	5.5
11.8	40	4.7	0	0.00	2	0.24	0	0.00	54	6.4	2	0.24	1	0.12	2.0	12.5
8.5	35.9	3.08	0.7	0.05	3	0.24	0.4	0.03	53.5	4.56	2.9	0.24	3.3	0.26	1.9	7 9
11.8	44	4.7	2	0.14	10	0.58	2	0.18	61	6.4	5	0.38	8	0.54	3.0	12.5
5.8	26	1.9	0	0.00	0	0.00	0	0.00	46	2.7	1	0.09	0	0.00	1.0	5.0
								Boys and Girls								
7.94	33.7	2.71	2.8	0.21	3.7	0.31	0.8	0.07	50.2	3.96	3.4	0.27	5.4	0.40	2.0	10.1
8.5	35.9	3.08	0.7	0.55	3	0.24	0.4	0.03	53.5	4.56	2.9	0.24	3.3	0.26	1.9	7.9
8.15	34.5	2.85	2	0.15	3.4	0.28	0.6	0,05	51.5	4.19	3.2	0.26	4.6	0.35	2.0	9 3
11.8	50	5.0	6	0.60	10	1.10	2	0.20	71	6.7	10	0.90	12	0.98	11.0	59.0
5.4	10	0.7	0	0.00	0	0.00	0	0.00	18	1.8	1	0.07	0	0.00	0.5	3.5

* Each section of tables 1 to 7 is divided into two parts, which are separated by a rule. The figures above the rule represent values for individual children; those in the three lines below the rule are (1) the average, (2) the highest and (3) the lowest of the individual values.

† In thousands.

‡ Polymorphonuclears.

§ Staff cells.

TABLE 2.—*Total, Differential and Absolute Leukocyte Counts and Sedimentation Rates for Children Nine Years Old* *

Leukocytes per Cu. Mm.†	Neutrophil Lobocytes		Neutrophil Rhabdocytes		Eosinophil Lobocytes		Basophil Lobocytes		Lymphocytes		Monocytes		Disintegrated Cells		Sedimentation Rate	
	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	Mm. in 15 Min.	Mm. in 45 Min.
								Boys								
3.4	26	0.9	2	0.07	4	0.14	1	0.03	58	2.0	2	0.07	6	0.20	0.5	2.5
5.3	46	2.4	2	0.11	4	0.21	1	0.05	33	1.7	6	0.32	7	0.37	2.0	11.0
6.4	24	1.5	4	0.26	3	0.19	0	0.00	61	3.9	4	0.26	4	0.26	1.0	4.0
7.6	33	2.5	2	0.15	0	0.00	2	0.15	58	4.4	2	0.15	3	0.23	1.0	2.0
8.4	22	1.8	1	0.80	6	0.50	1	0.08	67	5.6	1	0.08	2	0.17	0.5	3.0
8.4	56	4.7	2	0.17	6	0.50	0	0.00	23	1.9	3	0.25	10	0.84	1.5	5.5
9.1	38	3.5	1	0.09	8	0.73	0	0.00	46	4.2	4	0.36	2	0.18	1.5	3.5
9.3	57	5.3	6	0.56	2	0.17	1	0.09	23	2.1	5	0.46	6	0.56	3.0	26.0
9.4	49	4.6	0	0.00	2	0.19	0	0.19	44	4.1	3	0.28	0	0.00	0.5	4.0
9.5	25	2.4	2	0.19	4	0.38	1	0.10	55	5.2	2	0.19	11	1.04	1.0	4.5
9.8	49	4.8	1	0.10	5	0.49	0	0.00	40	3.9	2	0.20	2	0.20	3.0	19.0
10.8	31	3.3	8	0.86	1	0.11	0	0.00	49	5.3	2	0.22	9	0.97	1.5	3.5
11.2	42	4.7	0	0.00	0	0.00	1	0.11	53	6.0	2	0.22	2	0.22	1.5	9.0
16.1	66	10.6	8	1.29	0	0.00	0	0.00	13	2.1	5	0.80	8	1.29	16.0	62 0
8.9	40.3	3.78	2.8	0.28	3.2	0.26	0.7	0.06	44.5	3.74	3.1	0.28	5.1	0.47	2.5	11.4
16.1	66	10.6	8	1.29	8	0.73	2	0.19	67	6.0	6	0.80	11	1.29	16.0	62.0
3.4	22	0.9	0	0.00	0	0.00	0	0.00	13	1.7	1	0.07	0	0.00	0.5	2.0
								Girls								
5.3	40	2.1	14	0.74	4	0.21	0	0.00	34	1.8	4	0.21	4	0.21	1.0	6.5
5.6	32	1.8	1	0.06	2	0.11	1	0.06	58	3.2	3	0.17	3	0.17	1.5	4.0
6.6	44	2.9	5	0.33	3	0.20	1	0.07	36	2.4	5	0.33	6	0.40	10.0	50.0
7.2	63	4.5	2	0.14	1	0.07	2	0.14	26	1.9	3	0.22	3	0.22	1.5	5.0
7.4	40	3.0	1	0.07	4	0.30	0	0 00	50	3.7	2	0.15	3	0.22	1.0	3.5
7.9	37	2.9	0	0.00	2	0.16	1	0.08	58	4.6	1	0.08	1	0.08	2.0	18.5
9.4	36	3.4	4	0.38	1	0.09	0	0.00	52	4.9	2	0.19	5	0.47	2.0	14.0
11.0	50	5.5	0	0.00	6	0.66	1	0.11	38	4.2	1	0.11	4	0.44	1.5	7.0
13.2	56	7.4	1	0.13	2	0.26	0	0.00	38	5.0	0	0.00	3	0.40	1.5	3.5
18.7	45	8.4	2	0.37	1	0.19	1	0.19	48	9.0	2	0.37	1	0.19	Q. N. S.	Q. N. S.
9.23	44.3	4.19	3	0.22	2.6	0.22	0.7	0.06	43.8	4.07	2.3	0.18	3.3	0.28	2.4	12.4
18.7	63	8.4	14	0.74	6	0.66	2	0.19	58	9.0	5	0.37	6	0.47	10.0	50.0
5.3	32	1.8	0	0.00	1	0.07	0	0.00	26	1.8	0	0.00	1	0.08	1.0	3.5
								Boys and Girls								
8.9	40.3	3.78	2.8	0.28	3.2	0.26	0.7	0.06	44.5	3.74	3.1	0.28	5.1	0.47	2.5	11.4
9.2	44.3	4.19	3	0.22	2.6	0.22	0.7	0 06	43.8	4.07	2.3	0.18	3.3	0.28	2.4	12.4
9.07	42	3.96	2.9	0.26	3	0.24	0.7	0.06	44.2	3.88	2.8	0.24	4.4	0.39	2.4	11.8
18.7	66	10.6	14	1.29	8	0.73	2	0.19	67	9.0	6	0.80	11	1.29	16.0	62 0
3.4	22	0.9	0	0.00	0	0.00	0	0.00	13	1.7	0	0.00	0	0.00	0.5	2.0

* See footnote to table 1.
† In thousands.

TABLE 3.—*Total, Differential and Absolute Leukocyte Counts and Sedimentation Rates for Children Ten Years Old* *

Leukocytes per Cu. Mm.†	Neutrophil Lobocytes		Neutrophil Rhabdocytes		Eosinophil Lobocytes		Basophil Lobocytes		Lymphocytes		Monocytes		Disintegrated Cells		Sedimentation Rate	
	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	Mm. in 15 Min.	Mm. in 45 Min.
								Boys								
7.2	38	2.7	4	0.29	2	0.14	1	0.07	46	3.3	6	0.43	2	0.14	1.0	5.0
7.4	40	3.0	4	0.30	6	0.44	1	0.07	34	2.5	4	0.30	8	0.59	3.0	4.5
7.7	34	2.6	3	0.23	10	0.77	2	0.15	42	3.2	2	0.15	6	0.46	0.5	3.0
7.8	30	2.3	5	0.39	2	0.16	1	0.08	40	3.1	7	0.55	15	1.17	1.0	6.0
8.2	18	1.5	1	0.08	3	0.25	0	0.00	70	5.7	2	0.16	6	0.49	1.0	2.0
8.5	30	2.6	0	0.00	2	0.17	1	0.08	61	5.2	2	0.17	4	0.34	2.0	5.5
8.9	45	4.0	3	0.27	1	0.09	1	0.09	46	4.1	2	0.18	2	0.18	1.0	6.0
9.1	48	4.4	4	0.36	3	0.27	0	0.00	37	3.4	2	0.18	5	0.46	0.5	2 5
10.0	48	4.8	2	0.20	1	0.10	1	0.10	45	4.5	3	0.30	0	0.00	0.5	2.5
13.6	25	3.4	2	0.27	3	0.41	0	0.00	64	8.7	2	0.27	4	0.54	1.0	9.0
8.84	35.6	3.13	2.8	0.24	3.3	0.28	0.8	0.06	48.5	4.37	3.2	0.27	5.2	0.44	1.2	4.6
13.6	48	4.8	5	0.39	10	0.77	2	0.15	70	8.7	7	0.55	15	1.17	3.0	9.0
7.2	18	1.5	0	0.00	1	0.09	0	0.00	34	2.5	2	0.15	0	0.00	0.5	2.0
								Girls								
6.6	26	1.7	2	0.13	6	0.40	0	0.00	58	3.8	2	0.13	6	0.40	2.5	13 5
6.8	30	2.0	6	0.41	3	0.20	2	0.14	51	3.5	3	0.20	5	0.34	3.0	16.0
7.2	38	2.7	11	0.79	1	0.07	0	0 00	40	2.9	4	0.29	6	0.43	2.5	17.5
7.3	22	1.6	2	0.15	4	0.29	0	0.00	64	4.7	2	0.15	6	0.44	1.0	5.0
7.4	30	2.2	13	0.96	2	0.15	0	0.00	43	3.2	4	0.30	8	0.59	0.5	5.0
7.5	23	1.7	4	0.30	2	0.15	1	0.08	62	4.6	4	0.30	4	0.30	2.0	11.5
7.6	40	3.0	5	0.38	1	0.08	0	0.00	42	3.2	7	0.53	5	0.38	1.5	7.5
7.6	30	2.3	3	0.23	3	0.23	0	0.00	58	4.4	2	0.15	4	0.30	2.0	8.0
9.4	31	2.9	1	0.09	2	0.19	0	0.00	60	5.6	2	0.19	4	0.38	1.0	5.0
9.7	28	2.7	4	0.39	2	0.19	1	0.10	58	5.6	4	0.39	3	0.29	1.5	9.5
19.6	46	9.0	1	0.20	2	0.39	1	0.20	43	8.4	6	1.18	1	0.20	2.5	8.5
8.79	31.3	2.89	4.7	0.37	2.5	0.21	0.4	0.05	52.6	4.54	3.6	0.35	4.7	0.37	1.8	9.7
19.6	46	9.0	13	0.96	6	0.40	2	0.20	64	8.4	7	1.18	8	0.59	3.0	17.5
6.6	22	1.6	1	0.09	1	0.07	0	0.00	40	2.9	2	0.13	1	0.20	0.5	5.0
								Boys and Girls								
8.84	35.6	3.13	2.8	0.24	3.3	0.28	0.8	0 06	48.5	4.37	3.2	0.27	5.2	0.44	1.2	4.6
8.79	31.3	2.89	4.7	0.37	2.5	0.21	0.4	0.05	52.6	4.54	3.6	0.35	4.7	0.37	1.8	9 7
8.81	33.3	3.0	3.8	0.31	2.9	0.24	0.6	0.06	50.7	4.46	3.4	0.31	5	0.40	1.5	7.3
19.6	48	9.0	13	0.96	10	0.77	2	0 20	70	8.7	7	1.18	15	1.17	3.0	17 5
6.6	18	1.5	0	0.00	1	0.07	0	0.00	34	2.5	2	0.13	0	0.00	0.5	2.0

* See footnote to table 1.
† In thousands.

TABLE 4.—*Total, Differential and Absolute Leukocyte Counts and Sedimentation Rates for Children Eleven Years Old* *

Leukocytes per Cu. Mm.†	Neutrophil Lobocytes		Neutrophil Rhabdocytes		Eosinophil Lobocytes		Basophil Lobocytes		Lymphocytes		Monocytes		Disintegrated Cells		Sedimentation Rate	
	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	Mm. in 15 Min.	Mm. in 45 Min.
								Boys								
6.9	36	2.5	6	0.41	6	0.41	1	0.07	41	2.8	4	0.28	6	0.41	2.0	20.0
6.9	42	2.9	2	0.14	3	0.21	0	0.00	45	3.1	2	0.14	6	0.41	0.5	2.5
7.3	53	3.9	2	0.15	2	0.15	1	0.07	41	3.0	1	0.07	0	0.00	2.0	12.0
7.4	30	2.2	2	0.15	8	0.59	0	0.00	54	4.0	2	0.15	4	0.30	0.5	7.0
7.6	48	3.6	2	0.15	2	0.15	1	0.08	40	3.0	2	0.15	5	0.38	1.5	7.0
7.6	40	3.0	2	0.15	0	0.00	0	0.00	49	3.7	6	0.46	3	0.23	3.0	26.0
7.6	53	4.0	2	0.15	2	0.15	1	0.08	36	2.7	2	0.15	4	0.30	0.5	1.5
8.0	34	2.7	4	0.32	5	0.40	1	0.08	47	3.8	2	0.16	7	0.56	0.5	8.0
9.3	22	2.0	3	0.28	2	0.19	1	0.09	55	5.1	2	0.19	15	1.40	2.0	10.0
10.0	34	3.4	1	0.10	4	0.40	1	0.10	50	5.0	6	0.60	4	0.40	3.0	17.0
11.7	36	4.2	1	0.12	1	0.12	0	0.00	59	6.9	3	0.35	0	0.00	1.0	2.5
8.21	38.9	3.13	2.4	0.19	3.2	0.25	0.6	0.05	47	3.9	2.9	0.24	4.9	0.40	1.5	10.3
11.7	53	4.2	6	0.41	8	0.59	1	0.10	59	6.9	6	0.60	15	1.40	3.0	26.0
6.9	22	2.0	1	0.10	0	0.00	0	0.00	36	2.7	1	0.07	0	0.00	0.5	1.5
								Girls								
7.1	22	1.6	0	0.00	5	0.36	0	0.00	70	5.0	3	0.21	0	0.00	1.5	8.5
7.4	26	1.9	3	0.22	1	0.07	0	0.00	61	4.5	3	0.22	6	0.44	3.0	36.0
7.6	28	2.1	0	0.00	1	0.08	0	0.00	69	5.2	2	0.15	0	0.00	1.0	3.0
8.0	35	2.8	1	0.08	1	0.08	1	0.08	54	4.3	6	0.48	2	0.16	4.0	27.5
8.8	34	3.0	1	0.09	1	0.09	0	0.00	62	5.5	0	0.00	2	0.18	1.0	6.0
9.3	45	4.2	12	1.12	2	0.19	0	0.00	32	3.0	2	0.19	7	0.65	2.5	6.0
10.0	29	2.9	11	1.10	0	0.00	1	0.10	48	4.8	1	0.10	10	1.00	4.0	28.0
11.4	16	1.8	2	0.23	1	0.11	0	0.00	58	6.6	1	0.11	22	2.51	3.0	9.0
11.6	53	6.1	1	0.12	1	0.12	1	0.12	39	4.5	2	0.23	3	0.35	1.5	6 0
12.0	40	4.8	1	0.12	2	0.24	1	0.12	49	5.9	6	0.72	1	0.12	3.0	16.5
13.8	58	8.0	8	1.10	2	0.28	1	0.14	27	3.7	2	0.28	2	0.28	1.5	8.5
9.73	35.1	3.56	3.64	0.38	1.54	0.15	0.4	0 05	51.7	4.8	2.5	0.24	5	0.52	2.4	14.1
13.8	58	8.0	12	1.12	5	0.36	1	0.14	70	6.6	6	0.72	22	2.51	4.0	36.0
7.1	16	1.6	0	0.00	0	0.00	0	0.00	27	3.0	0	0.00	0	0.00	1.0	3.0
								Boys and Girls								
8.21	38.9	3.13	2.4	0.19	3.2	0.25	0.6	0.05	47	3.9	2.9	0.24	4.9	0.40	1.5	10.3
9.73	35.1	3.56	3.6	0.38	1.5	0.15	0.4	0.05	51.7	4.8	2.5	0.24	5	0.52	2.4	14.1
8.97	37	3.34	3	0.29	2.4	0.20	0.5	0.05	49.4	4.37	2.7	0.24	5	0.46	1.9	12.2
13.8	58	8.0	12	1.12	8	0.59	1	0.14	70	6.9	6	0.72	22	2.51	4.0	36.0
6.9	16	1.6	0	0.00	0	0.00	0	0.00	27	2.7	0	0.00	0	0.00	0.5	1.5

* See footnote to table 1.
† In thousands.

TABLE 5.—*Total, Differential and Absolute Leukocyte Counts and Sedimentation Rates for Children Twelve Years Old* *

Leukocytes per Cu. Mm.†	Neutrophil Lobocytes		Neutrophil Rhabdocytes		Eosinophil Lobocytes		Basophil Lobocytes		Lymphocytes		Monocytes		Disintegrated Cells		Sedimentation Rate	
	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	Mm. in 15 Min.	Mm. in 45 Min.
								Boys								
6.0	59	3.5	4	0.24	3	0.18	0	0.00	24	1.4	6	0.36	4	0.24	1.5	7.0
7.0	28	2.0	8	0.56	8	0.56	1	0.07	36	2.5	5	0.35	11	0.77	6.0	32.0
7.1	46	3.3	3	0.21	1	0.07	1	0.07	25	1.8	10	0.71	14	0.99	0.5	2.5
7.6	35	2.7	1	0.08	3	0.23	0	0.00	53	4.0	3	0.23	5	0.38	1.5	6.5
8.3	50	4.2	4	0.33	4	0.33	1	0.08	31	2.6	6	0.50	4	0.33	2.5	14.0
8.4	60	5.0	2	0.17	2	0.17	1	0.08	26	2.2	4	0.34	4	0.34	0.0	1.5
9.3	26	2.4	2	0.18	8	0.74	0	0.00	58	5.4	4	0.37	1	0.09	3.0	5.5
9.7	40	3.9	6	0.58	2	0.19	1	0.10	30	2.9	8	0.78	13	1.30	3.0	23.0
9.8	48	4.7	14	1.37	3	0.29	0	0.00	22	2.2	4	0.39	8	0.78	1.0	7.0
11.0	28	3.1	4	0.44	4	0.44	1	0.11	44	4.8	4	0.44	14	1.54	2.5	19.0
8.42	42	3.48	4.8	0.42	3.8	0.32	0.6	0.05	34.9	2.98	5.4	0.45	7.8	0.68	2.2	11.8
11.0	60	5.0	14	1.37	8	0.74	1	0.11	58	5.4	10	0.78	14	1.54	6.0	32.0
6.0	26	2.0	1	0.08	1	0.07	0	0.00	22	1.4	3	0.23	1	0.09	0.0	1.5
								Girls								
6.4	36	2.3	6	0.38	3	0.19	0	0.00	53	3.4	1	0.06	1	0.06	1.0	2.0
6.5	21	1.4	4	0.26	2	0.13	1	0.06	54	3.5	3	0.20	15	0.98	4.0	16.0
6.6	43	2.8	7	0.46	4	0.26	1	0.07	40	2.6	3	0.20	2	0.13	4.0	31.0
6.6	32	2.1	2	0.13	4	0.26	1	0.07	53	3.5	2	0.13	6	0.40	2.0	19.0
7.1	50	3.6	3	0.21	0	0.00	0	0.00	44	3.1	1	0.07	2	0.14	2.5	14.0
7.1	27	1.9	20	1.42	1	0.07	1	0.07	40	2.8	2	0.14	9	0.64	2.5	18.0
8.7	30	2.6	0	0.00	1	0.09	3	0.26	63	5.5	2	0.17	1	0.09	3.0	11.0
9.8	43	4.2	4	0.39	0	0.00	0	0.00	48	4.7	3	0.29	1	0.10	2.0	8.0
11.7	45	5.3	0	0.00	0	0.00	0	0.00	51	6.0	2	0.23	2	0.23	0.5	5.5
12.1	56	6.8	2	0.24	2	0.24	1	0.12	34	4.1	4	0.48	1	0.12	2.0	6.0
8.26	38.3	3.3	4.8	0.35	1.7	0.12	0.8	0.06	48	3.92	2.3	0.20	4	0.29	2.3	13.0
12.1	56	6.8	20	1.42	4	0.26	3	0.26	63	6.0	4	0.48	15	0.98	4.0	31.0
6.4	21	1.4	0	0.00	0	0.00	0	0.00	34	2.6	1	0.06	1	0.06	0.5	2.0
								Boys and Girls								
8.42	42	3.48	4.8	0.42	3.8	0.32	0.6	0.05	34.9	2.98	5.4	0.45	7.8	0.68	2.2	11.8
8.26	38.3	3.3	4.8	0.35	1.7	0.12	0.8	0.06	48	3.92	2.3	0.20	4	0.29	2.3	13.0
8.34	40.2	3.39	4.8	0.38	2.8	0.22	0.7	0.06	41.4	3.45	3.8	0.32	5.9	0.48	2.2	12.4
12.1	60	6.8	20	1.42	8	0.74	3	0.26	63	6.0	10	0.78	15	1.54	6.0	32.0
6.0	21	1.4	0	0.00	0	0.00	0	0.00	22	1.4	1	0.06	1	0.06	0.0	1.5

* See footnote to table 1.
† In thousands.

TABLE 6.—*Total, Differential and Absolute Leukocyte Counts and Sedimentation Rates for Children Thirteen Years Old*

Leukocytes per Cu. Mm.†	Neutrophil Lobocytes		Neutrophil Rhabdocytes		Eosinophil Lobocytes		Basophil Lobocytes		Lymphocytes		Monocytes		Disintegrated Cells		Sedimentation Rate	
	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	Mm. in 15 Min.	Mm. in 45 Min.
								Boys								
4.8	38	1.8	6	0.29	2	0.10	1	0.05	45	2.2	4	0.19	4	0.19	2.0	4.5
5.4	31	1.7	6	0.32	6	0.32	1	0.05	46	2.5	2	0.11	8	0.43	1.0	5.5
7.0	56	3.9	5	0.35	2	0.14	1	0.07	32	2.2	2	0.14	2	0.14	1.0	2.5
7.4	45	3.3	6	0.44	2	0.15	1	0.07	40	3.0	2	0.15	4	0.30	0.5	5.0
7.9	33	2.6	3	0.24	1	0.08	0	0.00	56	4.4	3	0.24	4	0.32	1.5	5.0
8.4	40	3.4	1	0.08	2	0.17	0	0.00	41	3.4	6	0.50	10	0.84	1.5	4.0
8.9	48	4.3	1	0.09	2	0.18	1	0.09	43	3.8	2	0.18	3	0.27	0.5	4.5
10.2	48	4.9	7	0.71	0	0.00	0	0.00	36	3.7	4	0.41	4	0.41	11.0	53.0
11.0	19	2.1	2	0.22	4	0.44	2	0.22	61	6.7	4	0.44	8	0.88	0.5	7.0
13.1	45	5.9	14	1.83	7	0.92	1	0.13	28	3.7	3	0.39	2	0.26	2.0	11.0
8.41	40.3	3.39	5.1	0.46	2.8	0.25	0.8	0.07	42.8	3.56	3.2	0.28	4.9	0.40	2.2	10.2
13.1	56	5.9	14	1.83	7	0.92	2	0.22	61	6.7	6	0.44	10	0.88	11.0	53.0
4.8	19	1.7	1	0.08	0	0.00	0	0.00	28	2.2	2	0.11	2	0.14	0.5	2.5
								Girls								
4.8	37	1.8	4	0.19	2	0.10	0	0.00	48	2.3	4	0.19	5	0.24	2.0	15.0
4.9	21	1.0	0	0.00	2	0.10	0	0.00	71	3.5	2	0.10	4	0.20	1.0	6.5
6.0	32	1.9	4	0.24	2	0.12	0	0.00	56	3.4	2	0.12	4	0.24	2.0	4.5
6.1	46	2.8	10	0.61	2	0.12	1	0.06	30	1.8	4	0.24	7	0.43	2.5	11.0
6.8	42	2.9	8	0.54	2	0.14	1	0.07	36	2.4	1	0.07	10	0.70	1.0	9.0
7.0	25	1.8	3	0.21	3	0.21	1	0.07	49	3.4	2	0.14	16	1.12	2.0	9.0
7.1	39	2.8	0	0.00	1	0.07	0	0.00	55	3.9	0	0.00	5	0.36	1.5	4.5
8.1	37	3.0	2	0.16	2	0.16	1	0.08	51	4.1	1	0.08	6	0.49	3.5	15.0
9.0	48	4.3	4	0.36	6	0.54	3	0.27	30	2.7	2	0.18	6	0.54	1.5	5.0
9.1	34	3.1	5	0.46	1	0.09	1	0.09	43	3.9	3	0.27	12	1.09	1.5	2.5
6.89	36.1	2.54	4	0.28	2.3	0.16	0.8	0.06	46.9	3.14	2.1	0.14	7.5	0.54	1.8	8.2
9.1	48	4.3	10	0.61	6	0.54	3	0.27	71	4.1	4	0.27	16	1.12	3.5	15.0
4.8	21	1.0	0	0.00	1	0.07	0	0.00	30	1.8	0	0.00	4	0.20	1.0	2.5
								Boys and Girls								
8.41	40.3	3.39	5.1	0.46	2.8	0.25	0.8	0.07	42.8	3.56	3.2	0.28	4.9	0.40	2.2	10.2
6.89	36.1	2.54	4	0.28	2.3	0.16	0.8	0.06	46.9	3.14	2.1	0.14	7.5	0.54	1.8	8.2
7.65	38.2	2.96	4.6	0.37	2.6	0.21	0.8	0.07	44.8	3.35	2.6	0.21	6.2	0.47	2.0	9.2
13.1	56	5.9	14	1.83	7	0.92	3	0.27	71	6.7	6	0.44	16	1.12	11.0	53.0
4.8	19	1.0	0	0.00	0	0.00	0	0.00	28	1.8	0	0.00	2	0.14	0.5	2.5

* See footnote to table 1.
† In thousands.

TABLE 7.—*Total, Differential and Absolute Leukocyte Counts and Sedimentation Rates for Children Fourteen Years Old* *

Leukocytes per Cu. Mm.†	Neutrophil Lobocytes		Neutrophil Rhabdocytes		Eosinophil Lobocytes		Basophil Lobocytes		Lymphocytes		Monocytes		Disintegrated Cells		Sedimentation Rate	
	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	Mm. in 15 Min.	Mm. in 45 Min.
								Boys								
5.4	29	1.6	1	0.05	0	0.00	0	0.00	61	3 3	2	0.11	7	0.38	0.5	1.5
6.4	22	1.4	1	0.06	2	0.13	0	0.00	66	4.2	2	0.13	6	0.38	1.0	3.5
6.7	56	3.8	1	0.07	3	0.20	0	0.00	33	2.2	4	0.27	3	0.20	7.5	41.5
7.1	38	2.7	1	0.07	2	0.14	0	0.00	54	3.8	3	0.21	2	0.14	5.0	22.0
7.3	26	1.9	0	0.00	1	0.07	1	0.07	63	4.6	4	0.29	5	0.36	2.0	15.0
7.4	27	2.0	2	0.15	0	0.00	1	0 07	64	4.7	1	0.07	5	0.37	1.0	2.5
7.4	47	3.5	1	0.07	3	0.22	1	0.07	40	3.0	4	0.30	4	0.30	1.5	2.5
7.9	44	3.5	0	0.00	5	0.40	0	0.00	46	3.6	4	0.32	1	0.08	2.0	8.5
9.5	30	2.8	0	0.00	2	0.19	0	0 00	62	5.9	1	0.10	5	0.48	0.5	1.0
10.0	28	2.8	2	0.20	4	0.40	1	0.10	56	5.6	6	0.60	3	0.30	0.0	2.0
11.0	51	5.6	1	0.11	2	0.22	0	0.00	42	4.6	2	0.22	2	0.22	3.0	16.0
12.9	44	5.7	4	0.52	1	0.13	1	0 13	41	5.3	5	0.64	4	0.52	1.5	3.0
8.25	36.8	3.11	1.2	0.11	2.1	0.18	0.4	0.04	52.3	4.23	3.2	0.27	3.9	0.31	2.1	9.9
12.9	56	5.7	4	0.52	5	0.40	1	0.13	66	5.9	6	0.64	7	0.52	7.5	41.5
5.4	22	1.4	0	0.00	0	0.00	0	0 00	33	2.2	1	0.07	1	0.08	0.0	1.0
								Boys and Girls								
5.6	42	2.4	0	0.00	1	0.06	1	0.06	50	2.8	4	0.22	2	0.11	1.0	8.5
7.0	52	3.6	0	0.00	0	0.00	1	0.07	39	2.7	2	0.14	5	0.35	2.0	5.0
7.2	40	2.9	4	0.29	1	0.07	1	0 07	50	3.6	2	0.14	1	0.07	0.5	1.0
7.4	21	1.6	1	0.07	1	0.07	1	0.07	65	4.8	2	0.15	7	0.52	1.5	12.0
7.5	36	2.7	2	0.15	6	0.45	2	0.15	44	3.3	4	0.30	5	0.38	14.0	60.0
8.0	38	3.0	1	0.08	5	0.40	2	0 16	44	3.5	6	0.48	4	0.32	1.5	6.0
9.0	35	3.2	1	0.09	0	0.00	0	0 00	59	5.3	2	0.18	3	0.27	2.0	13.0
9.2	48	4.4	1	0.09	1	0.09	1	0.09	41	3.8	6	0.55	2	0.18	1.0	3 0
11.0	54	5.9	1	0.11	1	0.11	1	0.11	36	4.0	4	0.44	3	0.33	2.5	20.0
12.0	35	4.2	2	0.24	2	0.24	0	0 00	55	6.6	2	0.24	4	0.48	0.5	7.0
8.39	40.1	3.39	1.3	0.11	1.8	0.15	1.0	0.08	48.3	4.04	3.4	0.28	3.6	0.30	2.6	13.6
12.0	54	5.9	4	0 29	6	0.45	2	0.16	65	6.6	6	0.55	7	0.52	14.0	60.0
5.6	21	1.6	0	0.00	0	0.00	0	0.00	36	2.7	2	0.14	1	0.07	0.5	1.0
								Girls								
8.25	36.8	3.11	1.2	0.11	2.1	0.18	0.4	0.04	52.3	4.23	3.2	0.27	3.9	0.31	2.1	9.9
8.39	40.1	3.39	1.3	0.11	1.8	0.15	1	0.08	48.3	4.04	3.4	0.28	3.6	0.30	2.6	13.6
8.31	38.3	3.24	1.2	0.11	2	0.16	0.7	0.06	50.5	4.14	3.3	0.28	3.8	0.31	2.4	11.6
12.9	56	5.9	4	0.52	6	0.45	2	0.16	66	6.6	6	0.64	7	0.52	14.0	60.0
5.4	21	1.4	0	0.00	0	0.00	0	0.00	33	2.2	1	0.07	1	0.07	0.0	1.0

* See footnote to table 1.
† In thousands.

TABLE 8.—*Summary of Tables One to Seven, the Total, Differential and Absolute Leukocyte Counts and Sedimentation Rates for Children Eight to Fourteen Years of Age* *

Age	No. of Cases	Leukocytes per Cu. Mm.†	Neutrophil Lobocytes		Neutrophil Rhabdocytes		Eosinophil Lobocytes		Basophil Lobocytes		Lymphocytes		Monocytes		Disintegrated Cells		Sedimentation Rate	
			%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	%	Per Cu. Mm.†	Mm. in 15 Min.	Mm. in 45 Min.
Boys																		
8	16	7.94	33.7	2.71	2.8	0.21	3.7	0.31	0.8	0.07	50.2	3.96	3.4	0.27	5.4	0.40	2.0	10.1
9	14	8.91	40.3	3.78	2.8	0.28	3.2	0.26	0.7	0.06	44.5	3.74	3.1	0.28	5.1	0.47	2.5	11.4
10	10	8.84	35.6	3.13	2.8	0.24	3 3	0.28	0.8	0.06	48.5	4.37	3.2	0.27	5.2	0.44	1.2	4 6
11	11	8.21	38.9	3.13	2.4	0.19	3.2	0.25	0.6	0.05	47.0	3.92	2.9	0.24	4.9	0.40	1.5	10.3
12	10	8.42	42.0	3.48	4.8	0.42	3.8	0.32	0.6	0.05	34.9	2.98	5.4	0.45	7.8	0.68	2.2	11.8
13	10	8.41	40.3	3.39	5.1	0.46	2.8	0.25	0 8	0 07	42.8	3.56	3.2	0.28	4.9	0.40	2.2	10.2
14	12	8.25	36.8	3.11	1.2	0.11	2.1	0.18	0.4	0 04	52.3	4.23	3.2	0.27	3.9	0.31	2.1	9.9
	83	8.41	38 0	3.23	3.0	0.26	3.2	0.26	0.7	0.06	46.2	3.84	3.4	0.29	5.3	0.44	2.0	9.9
		16.1	66.0	10.6	14.0	1.83	10.0	1.10	2.0	0 22	71.0	8.7	10.0	0.90	15.0	1.54	16.0	62 0
		3.4	10.0	0.7	0.0	0.00	0.0	0.00	0.0	0.00	13.0	1.4	1.0	0.07	0.0	0.00	0.0	1.0
Girls																		
8	10	8.50	35.9	3.08	0.7	0.05	3.0	0.24	0.4	0.03	53.5	4.56	2.9	0.24	3.3	0.26	1.9‡	7 9‡
9	10	9.23	44.3	4.19	3.0	0.22	2.6	0.22	0.7	0.06	43.8	4.07	2.3	0.18	3.3	0.28	2.4‡	12.4‡
10	11	8.79	31.3	2.89	4.7	0.37	2.5	0.21	0.4	0 05	52.6	4.54	3.6	0.35	4.7	0.37	1.8	9.7
11	11	9.73	35.1	3.56	3.6	0.38	1.5	0.15	0.4	0 05	51.7	4.82	2.5	0.24	5.0	0.52	2.4	14.1
12	10	8.26	38.3	3.30	4.8	0.35	1.7	0.12	0.8	0.06	48.0	3.92	2.3	0.20	4.0	0.29	2.3	13.0
13	10	6.89	36.1	2.54	4.0	0.28	2.3	0.16	0.8	0.06	46.9	3.14	2.1	0.14	7.5	0.54	1.8	8.2
14	10	8.39	40.1	3.39	1.3	0.11	1.8	0.15	1.0	0.08	48.3	4.04	3.4	0.28	3.6	0.30	2.6	13.6
	72	8.56	37 2	3.28	3.2	0.26	2.2	0.18	0.6	0.06	49.4	4.17	2.8	0.24	4.5	0.37	2.2§	11.3§
		19.6	63.0	9.00	20.0	1.42	10.0	0.66	3.0	0.27	71.0	9.00	7.0	1.18	22.0	2.51	14 0	60.0
		4.8	16.0	1.00	0.0	0.00	0.0	0.00	0.0	0.00	26.0	1.80	0.0	0.00	0.0	0.00	0.5	1.0
Boys and Girls																		
	83	8.41	38.0	3.23	3.0	0.26	3.2	0.26	0.7	0.06	46.2	3.84	3.4	0.29	5.3	0.44	2.0	9.9
	72	8.56	37.2	3.28	3.2	0.26	2.2	0.18	0 6	0 06	49.4	4.17	2.8	0.24	4.5	0.37	2.2§	11.3§
	155	8.48	37.6	3.25	3.1	0.26	2.7	0.22	0.7	0 06	47.6	3.99	3.1	0.26	4.9	0.40	2.1‖	10.5‖
		19.6	66.0	10.6	20.0	1.83	10.0	1.10	3.0	0 27	71.0	9.00	10.0	1.18	22.0	2.51	16.0	62.0
		3.4	10.0	0.7	0.0	0.00	0.0	0.00	0.0	0 00	13.0	1.40	0.0	0.00	0.0	0.00	0.0	1.0

* The figures above the rule are the averages given in tables 1 to 7; those below are the average, the highest and the lowest value found for the age group as a whole (8 to 14 years).

† In thousands.

‡ For 9 cases.

§ For 70 cases.

‖ For 153 cases.

RESULTS

Tables 1 to 7 summarize the individual results for the total, differential and absolute leukocyte counts and sedimentation rates for each age and sex group. From these tables and from the scatter diagrams [1d] it is evident that there is no significant difference arising from age or sex within this group, so that it is justifiable to summarize the results for the entire group as has been done in table 8. This table gives the averages and the extreme ranges. For clinical purposes, however, the most useful range of normal is not the extreme range but that range which will include about plus or minus three probable errors, or 95

TABLE 9.—*Statistical and Smoothed Means and Ranges of Total, Differential and Absolute Leukocyte Counts and Sedimentation Rates for Children Eight to Fourteen Years of Age*

		Statistical Mean	Probable Error, Distribution	Smoothed Mean	95% Range
Leukocytes*	Per Cu. Mm.	8,370 ± 91	1,541 ± 47	8,400	4,000-13,000
Neutrophil lobocytes	%	37.5 ± 0.6	7.1 ± 0.2†	38‡	16-60‡
	Per Cu. Mm.	3,242 ± 86	Skew	3,250	1,500-6,500
Neutrophil rhabdocytes	%	.....	.....	3‡	0-10‡
	Per Cu. Mm.	.....	.....	250‡	0-1,000‡
Eosinophil lobocytes	%	.....	.....	3‡	0-8‡
	Per Cu. Mm.	.....	.....	200	0-600
Basophil lobocytes	%	.....	.....	0.5§	0-2§
	Per Cu. Mm.	.....	.....	50§	0-200§
Lymphocytes	%	47.7 ± 0.6	8.0 ± 0.2	48‡	20-70‡
	Per Cu. Mm.	4,047 ± 76	Skew	4,000	1,500-6,500
Monocytes	%	.....	.....	3‡	0-7‡
	Per Cu. Mm.	.....	.....	300§	0-800§
Disintegrated cells	%	.....	.....	5‡	0-12‡
		.....	.....	400‡	0-1,200‡
Sedimentation rate	Mm. in 15 Min.	Skew	.....	2.0§	0.5-5.0§
	Mm. in 45 Min.	Skew	.....	10.0§	1.0-30.0§

* Ages 8 to 18.
† Applies also to persons 20 years of age and over.
‡ Applies also to children 4 to 7 years of age.
§ Applies to all persons over 4 years of age.

per cent of healthy persons. In other words, if a result in a child of this age group falls outside of this range there is less than one chance in twenty that it is normal for that child. These 95 per cent ranges are summarized in table 9.

COMMENT

The differential and absolute cell counts show a higher proportion of lymphocytes and a lower proportion of neutrophil lobocytes (polymorphonuclears) than have usually been given. The probable explanation for this is that most of the data previously reported have not been obtained from studies of strictly healthy persons. The percentages of lymphocytes and neutrophils are the same as those for children 4 to 7 years of age,[1e] but the percentage of lymphocytes is higher and the

percentage of neutrophils is lower than that for adolescents [1f] or for adults.[1g] The percentage of eosinophils is slightly higher than that for adolescents [1f] or for adults.[1g] The percentage of monocytes is slightly lower than that for adolescents [1e] or for adults.[1g]

The sedimentation rates form a skew curve, with the greater number of determinations falling in the lower ranges. It is probable that the rate of 15 mm. in forty-five minutes, which tops 80 per cent of the results, represents the strict upper limit of normal and that the higher rates are due to mild chronic infection in the tonsils, teeth or sinuses not detectable in the routine physical examination.

SUMMARY

There are no significant age or sex differences in the total, differential or absolute leukocyte counts or in the sedimentation rates for children 8 to 14 years of age. Table 9 gives the data which should be most useful in the interpretation of each of these determinations for children of this age group.

EFFECT OF A DIETARY SUPPLEMENT ON OSSIFICATION OF THE BONES OF THE WRIST IN INSTITUTIONAL CHILDREN

II. EFFECT OF A COD LIVER OIL SUPPLEMENT

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This investigation is one of a series undertaken to determine the response of bone growth in children to an improvement in nutrition. Ossification in the bones of the wrist has been the criterion of bone development; several food supplements have been used to improve nutrition. The effect of the daily addition to an institutional diet of a pint (473 cc.) of milk, plain or irradiated, was described in a previous article.[1] The present report concerns the effect of another supplement, cod liver oil.

The plan in the several studies was to find out under experimental conditions whether the rate of ossification would be modified by a dietary supplement in a group of children who were considered an average sample and who were receiving average diets. The striking effect of some specific supplements in cases of obvious deficiency diseases, such as rickets, is well known. As quality of bone may be an indication of previous nutritional history, a definite change in rate of ossification might be expected in response to improved nutrition even when to all outward appearance there had been no change.

In the earlier study milk was an appropriate addition to a diet which had previously averaged between a cup and a pint of milk per child daily and which was correspondingly poor in other protective foods. The children in the study were divided into three comparable groups, one continuing to receive the institutional diet, one receiving an additional pint of reconstituted evaporated milk and one an additional pint of irradiated evaporated milk per child per day. One of the somewhat unexpected results was that, while the groups given milk made signifi-

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This paper is numbered "II" because it is the second in a series of studies on ossification. The first paper in this series is that cited in footnote 1 (which was paper II of a series of studies of the physical status of a group of children).

1. MacNair, V., and Roberts, L. J.: Effect of a Milk Supplement on the Physical Status of Institutional Children: II. Ossification of the Bones of the Wrist, Am. J. Dis. Child. **56**:494 (Sept.) 1938.

cantly better gains in ossification than the control group, there was no appreciable difference between the advance made by those who had plain milk and those who had irradiated milk. One of several possible reasons for this may have been that the additional pint of irradiated milk added but 70 units of vitamin D a day. The effect of the other milk constituents, for which there was great need, may have obscured the effect of the vitamin. The question naturally arose as to what effect vitamin D might have on rate of growth in normal bone if given in such a way as to make possible more specific measurement of its effects.

Cod liver oil was a logical supplement to the diet in the second study for several reasons. First, it emphasized the addition of vitamin D. The daily dessert spoonful of cod liver oil which was given each child contributed approximately ten times the amount of this vitamin contained in the pint of irradiated milk. It also increased the vitamin A three or more times. Second, the regular diet of the homes chosen for the study on cod liver oil, while it was not perfect, was much better than that of the first institution. Milk was a substantial part of the diet, while fruits and vegetables were served the year around. The added cod liver oil, then, was somewhat more specific in this case than the milk which supplied many essentials deficient in the previous diet. Cod liver oil was also an appropriate supplement in the Chicago area, which is thoroughly blanketed from the potent rays of the sun for a considerable part of the year. The homes of the children of this study were within the confines of the city. The study on milk was done in a home outside Chicago, where the air is comparatively clear.

That there is a relation of nutrition to quality and growth of bone is well known. In cases of extreme deficiency, such as rickets, in which diet alone may remedy the defective calcification and change in quality may be watched by roentgen study, there is some difference of opinion as to the effect on rate of development. Most investigators have stated the belief that the rate is more or less decreased by rickets, the change depending on the severity and duration of the disease. With children the problem is complicated by the fact that a deficiency causing rickets is likely to be accompanied by other deficiencies, which may influence growth. The condition not so extreme as to show outwardly or to be classed with the deficiency diseases but manifesting the type of difference in quality and growth of bone with which this study is concerned was described by Sherman:[2]

> . . . growing children whose height, weight and appearance are normal, may have a calcium-poor condition of body which even the best physical examination

2. Sherman, H. C.: Chemistry of Food and Nutrition, ed. 5, New York, The Macmillan Company, 1937.

cannot reveal, but which is revealed by the chemical evidence of the calcium balance experiments determined directly upon children of different ages and fully confirmed by analyses of the bodies of experimental animals.

Is there in these cases, accompanying the calcium-poor condition, a corresponding change in rate of bony development? In this less extreme condition will the rate of ossification parallel the quality of bone which has been determined by the nutritional history, or will it continue at a nearly normal rate, as might be expected from the work of Jackson and Stewart [3] and others on rats, Aron on dogs [4] and Waters [5] on calves? These workers found that when a deficient diet was fed which just allowed the weight to be maintained, growth in length of the skeleton continued for some time at the expense of first the fatty tissue and then the muscles. Cammerer,[6] Morgulis [7] and others reported a similar kind of growth in malnourished young children, that is, increase in length with accompanying slenderness of form and poor muscular development. If in cases like these the skeleton continues to grow for a time, it could be expected to maintain a nearly normal rate under much less serious conditions.

Nutrition could be expected to affect rate of ossification as well as quality. The effect of socioeconomic status, which has been studied and discussed by Stettner,[8] Todd [9] and others, carries an implication of nutritional factors. Stettner, studying development of German children by means of roentgenograms of the hand, reported a difference in the quantity and quality of ossification in children of laborers, rural children and urban children of the middle class, the last having the best quality and highest rate of osseous growth. He suggested that hygienic conditions should be studied in connection with these differ-

3. Jackson, C. M., and Stewart, C. A.: Effect of Underfeeding and Refeeding upon the Growth of Various Systems in the Body, J. Exper. Zoöl. **30**:97, 1920.

4. Aron, H.: Nutrition and Growth, Philippine J. Sc. (Sect. B) **6**:1, 1911.

5. Waters, H. J.: The Capacity of Animals to Grow Under Adverse Conditions, Proc. Soc. Promotion Agric. Sc. **29**:3, 1908; **30**:70, 1909.

6. Cammerer, W.: Untersuchungen über Massenwachstum und Langerwachstum der Kinder, Jahrb. f. Kinderh. **36**:249, 1893.

7. Morgulis, S.: Fasting and Undernutrition, New York, E. P. Dutton & Company, 1923, pp. 289-308.

8. Stettner, E.: Ueber die Beziehungen der Ossification des Handskeletts zu Alter und Längenwachstum bei gesunden und kranken Kindern von der Geburt bis zur Pubertät, Arch. f. Kinderh. **68**:342 and 439, 1920; **69**:27, 1921; **70**:69, 1922; Ossificationsstudien am Handskelet: III. Die "physiologische Osteoporose," Ztschr. f. Kinderh. **52**:1, 1932.

9. Todd, T. W.: Roentgenographic Appraisement of Developmental Growth in the Skeleton, in Growth and Development of the Child: IV. Appraisement of the Child, White House Conference on Child Health and Protection, New York, Century Company, 1932, pp. 258-285.

ences. Wallis [10] found evidence that in three groups of young children with almost identical economic background and diverse European origin the amount of growth was the same, which indicated that the factors in the socioeconomic status in these cases were more potent than heredity in determining rate. Todd [11] stated the opinion that nutrition may explain, in part at least, the different norms for osseous development that he found in four classes of children. The most advanced were those of children who won a school health contest; in decreasing order followed the norms for average school children of Cleveland, children of low economic status and children who had died from causes other than accident.

Other tendencies of growth relevant to the present study have been noted. Baldwin [12] stated that between 6 and 17 years of age children under poor nutritional conditions grow as fast or faster than well nourished children, but before that time they are shorter and hence never attain to equal height. Moreover, according to Flory,[13] there appears to be a tendency at the time of puberty for bone to mature and for the area of the wrist to more or less fill with bones articulated as in the adult, whatever the previous lag. This does not mean that there may not be a continuing lag due to external causes, but there seems to be a tendency to mature with the materials at hand, whatever they are. This, of course, correlates with the evidence that less well nourished people are of smaller adult stature.

The retarding effect of illness, especially fevers, on rate of bony development has been noted by several authors, with a suggestion that it may be through disturbance of nutritional processes that the retardation is effected. Pryor [14] stated that "conditions of health, accidents, disease, anything that would interfere with the blood supply or modify metabolism would be likely to delay or modify the process of ossification." Rotch [15] also stated that epiphysial development can be affected only by normal or abnormal changes in metabolism. Todd [9] listed such disorders as diarrhea, measles, whooping cough and mumps as likely

10. Wallis, R. S.: How Children Grow, Studies in Child Welfare, Iowa City, University of Iowa, 1931.

11. Todd, T. W.: Human Bodies and Human Beings, Sigma Xi Quart. **21**: 123, 1933.

12. Baldwin, B. T.: Physical Growth and School Progress, Bulletin 10, United States Department of the Interior, Bureau of Education, 1914.

13. Flory, C. D.: Osseous Development in the Hand as an Index of Skeletal Development, Monographs of the Society for Research in Child Development, National Research Council, 1936, vol. 1, no. 30.

14. Pryor, J. W.: Some Observations on the Ossification of Bones in the Hand, Bull. Univ. Kentucky (no. 11) **8**:1, 1916.

15. Rotch, T. M.: Roentgen Ray Methods Applied to the Grading of Early Life, Am. Phys. Educ. Rev. **15**:396, 1910.

to cause delay in the appearance of the carpal centers and indicated a possible relation of the delay to disturbance of the nutritional condition by the disease.

The close interrelation of the factors which may affect metabolism or nutrition and therefore development of bone, in the opinion of workers who have studied this phase of growth, is shown by the observation of Wallis [10] on a group of children whose growth, anthropometric and osseous, she followed for several years. She said of them:

> . . . these children belong to a favored class whose economic environment offers the possibility of attaining the maximum growth inherent in their family lines. . . . Very few do not receive optimum diet throughout the year. . . . Careful school health programs have greatly reduced the spread of contagious diseases which result in retardation of growth.

Flory found that recent norms for the Carter ossification ratio obtained from children of the University of Chicago Laboratory School were higher than those obtained from the same group thirteen to fifteen years ago. He suggested the explanation that in the last decade nutritional management in this group has been significantly improved with a wholesome effect on the osseous growth of the subjects, which affected the average for their age. Again, in discussing some of the studies of ossification which have been made, Flory said that if retardation can occur only when disease is present, then in some children there must be hidden disorders which are not detected by the ordinary medical examination. And later he stated that "the nutritional aspect of the problem needs further investigation."

There have been very few studies of the relation of calcium and vitamin D to growth in human beings in whom various aspects of growth, including skeletal, were followed quantitatively. Daniels, Hutton, Stearns and Hejinian,[16] studying the relation of the rate of growth in infants to diet from the standpoint of physical measurements and nitrogen metabolism, found that children receiving cod liver oil grew at a more rapid rate than children given the same diet without cod liver oil. The physical measurements included growth in length, which is one aspect of skeletal growth. Jeans, Stearns and their co-workers studied a series of infants throughout the major portion of infancy (as reported by Jeans [17]). They obtained comprehensive data on intakes of milk and vitamin D, calcium and phosphorus retention, levels of

16. Daniels, A. L.; Hutton, M. K.; Stearns, G., and Hejinian, L. M.: The Relation of Rate of Growth in Infants to Diet, Am. J. Dis. Child. **37**:1177 (June) 1929.

17. Jeans, P. C.: Vitamin D Milk: The Relative Value of Different Varieties of Vitamin D Milk for Infants; a Critical Interpretative Review, J. A. M. A. **106**:2066 (June 13); 2150 (June 20) 1936.

calcium and phosphorus in the serum, linear growth and increases in weight, dentition, motor achievement, and ossification as shown by a series of roentgenograms of a wrist of each infant. There were three divisions: groups 1 and 2 received whole acidified fresh and evaporated milk, respectively, and 340 units of vitamin D daily, with orange juice and sieved vegetables and fruits; group 3 received the same foods but only 60 to 135 units of vitamin D a day. The results of the study were given by Jeans:

> The serum calcium and phosphorus values in all three groups were normal. . . . Each infant in groups 1 and 2 grew both in length and in weight at greater than the average rate; dentition was early, most of the infants having cut two teeth by 6 months of age and six teeth by 9 months of age. No infant attained the age of 8 months without having cut at least two teeth. Carpal centers became visible to the X-rays more rapidly than usual. The infants were physically very active. The majority were able to sit unsupported by 6 months of age and could pull themselves to standing by 9 months. In short, the infants of these two groups were superb physical specimens. The retentions of calcium, phosphorus and nitrogen were very high, indicating that, notwithstanding the rapid growth, the mineralisation of bones and the muscular development were above the average.
>
> The rate of growth of the infants of group 3 was much slower than that of the babies in the other two groups, although it could be considered "average." Dentition was late; most of the infants did not begin cutting teeth until 8 or more months of age. None of these infants were able to sit unsupported at 9 months of age; two were able to do so by 10 months, but the muscles were flaccid and the posture poor. The retentions of calcium and phosphorus by the babies of this third group was much less than in the babies of groups 1 and 2; so much less that the slower rate of growth did not compensate, and the retention per kilogram of weight increase and per centimeter of growth in length was definitely lower than the retention for the babies of groups 1 and 2.

This work is of particular interest here, first, because in it the effect of diet on skeletal development was studied by relating linear growth and the appearance of the carpals to a dietary constituent under consideration in this study; second, because the two groups of children, not suffering from obvious deficiency disease but differing in quality of growth, were similar to the groups of children with which we are concerned in the present series of studies.

A few investigators, then, have reported studies which suggest in varying degrees and several ways that nutritional status must be included among the influences governing quantity as well as quality of osseous growth.

The purpose of this series of studies, as indicated earlier, was to observe under conditions carefully controlled the effect of nutritional status on the rate of bone growth and to determine its magnitude as shown by measurement of the advance in ossification in the carpal area.

METHODS

The subjects of this study lived in several homes for children in Chicago and were between the ages of 2.5 and 10.5 years. This age range was chosen for several reasons. Before adolescence bone development is more rapid, and individuals vary less, than during adolescence. In addition, "as the child grows older, he becomes far less susceptible than in early life to the effect of those influences that disrupt skeletal maturity."[9] Then, too, the Carter ossification ratio used in these studies to assess skeletal development gives a better picture during preadolescent ages than during the teen ages (Flory[13]). Therefore the decision was made to use preadolescent children for the study on cod liver oil. Administration of cod liver oil to one of two matched groups of children was started early in March 1935. The groups were formed of partners in matched pairs, which were chosen after study of 117 roentgenograms, 56 of boys and 61 of girls, taken in February. By means of these initial roentgenograms, 52 pairs of children were matched for sex, skeletal maturity and chronologic age. There were 24 pairs of boys and 28 of girls. One of each pair received the institutional diet with no addition, and the other received a daily dessertspoonful of cod liver oil besides the regular diet. This amount of cod liver oil added approximately 700 units of vitamin D and 4,500 units of vitamin A.

In the year this study was made, February 1935 to March 1936, the usual turnover in such homes was exceeded, as it was a year of recovery and children were returning to reestablished homes. Therefore by the end of the year many pairs had lost a partner. There remained at the end 83 of the original 117 children. Fifteen of these, 6 control and 9 experimental girls living in a small home, were dropped because there had been changes which made the groups hardly comparable. In the second home no well matched partners were left, but the control and the experimental group, consisting of 7 and 8 children, respectively, were still comparable. In a larger home there remained 53 children, including 19 pairs matched for initial skeletal development. The data obtained from the 19 pairs will be presented in some detail.

The home in which the 19 pairs lived is one of the best of its kind. The dietitian in charge of the food supply is interested in the growth of the children and keeps monthly records of weight. Before and during the study each child received two half-pint bottles of milk per day in the summer and three during the winter months, in addition to the milk used in cooking. The intention of the management of the institution is that every child shall average a quart of milk per day. Fruits and vegetables are a regular part of the diet. A graduate nurse has charge of the dispensary and of the well equipped infirmary, and there is a regularly attending physician. Varied backgrounds are represented among the children, who are of foreign or American ancestry and of poor or middle class families; usually the parents have separated, or only one is left to support the child. Very few of the children are orphans.

The graduate nurse was responsible for the administration of the cod liver oil. To a number of the children living in the main building she herself gave the daily dessertspoonful. When matrons in the cottages administered the oil, she supplied them with the oil and through frequent contact supervised the dosage and the keeping of records. In the infirmary records were kept of illnesses, medicines or special diets given and of absences at city hospitals. A record of the administration of cod liver oil was added for the period of the study. The policy was to disturb the regular routine of the institution as little as possible. The

person in charge of the project (V. M.) was in constant personal contact with the staff and home, taking the monthly weights with the dietitian and having frequent conferences with the nurse and superintendent.

The development of bone in the wrist was followed by means of roentgenograms of the right hand and forearm. The method of taking and measuring the roentgenograms has been described in some detail in a previous report.[1] The essentials will be reviewed briefly here. When the roentgenograms were taken, special care was exercised to have them uniform in regard to position of wrist and distance from the target. The exposure was adjusted as accurately as possible to the size and development of the hand in order that the films might have comparable density. The area of the wrist was chosen for study because (1) ossification in the hand and forearm has been shown to be representative of that in other parts of the skeleton, (2) uniform roentgenograms of this area are comparatively easy to obtain, and (3) the most comprehensive norms of skeletal development available are based on measurement of these centers.

Two methods of assessing bone development were used, as in the previous study. The first, a qualitative method (which includes quantitative aspects) employing the Flory inspectional age scale, matched children for development

TABLE 1.—*Initial Mean Carter Indexes and Chronologic Ages of the Control and the Experimental Group Previously Matched as to Development Toward Maturity*

Group	Carter Index, Ossification Ratio		Chronologic Age, Years	
	Boys	Girls	Boys	Girls
Control	36.8	59.5	6.2	7.3
Experimental	38.3	57.8	6.4	7.5

toward the mature form.[13] The second, a quantitative method utilizing the Carter ossification ratio, was used to determine and to compare increments of growth objectively.[18] This ratio, or index, relates the sum of the areas of the roentgen shadows of the carpal bones and the epiphyses of the radius and the ulna to the area of the wrist, i. e., the area ossified to the area to be ossified:

$$\frac{\text{Sum of areas of carpal bones}}{\text{Area of carpal quadrilateral}} = \text{Carter index, or ossification ratio.}$$

The areas are obtained by circumscribing with a planimeter the shadows of the carpal bones and also the outline of a designated quadrilateral which represents the wrist.

As soon as the initial roentgenograms were measured according to the Carter technic, the partners as tentatively set up by the Flory skeletal age were rechecked by the Carter ossification ratio with the intention of making any shifts necessary for matching them on this basis as well. No shifts were found necessary, however. This might be expected in view of the fact that the ossification ratio and the inspectional age have been shown by Flory to correlate, the respective figures for boys and girls being 0.833 ± 0.024 and 0.884 ± 0.023 for these ages. The small differences between partners balanced each other, and the means for the two groups are therefore fairly close, as is shown in table 1. The mean Carter indexes for

18. Freeman, F. N., and Carter, T. M.: A New Measurement of the Development of the Carpal Bones and Its Relation to Physical and Mental Development, J. Educ. Psychol. **15**:257, 1924.

children in the control and the experimental group are 36.8 and 38.3 for boys and 59.5 and 57.8 for girls, respectively. Mean chronologic ages are similarly close, being 6.3 and 6.4 years for boys and 7.3 and 7.5 for girls in the control and the experimental group, respectively.

RESULTS

Before the data from this study are presented, it is appropriate to consider what might be expected as a result of adding cod liver oil to the diet of these children. It was mentioned earlier that protective foods were well represented in the institutional diet. Milk, vegetables and fruits were served regularly. The total amount of food seemed liberal. Therefore it is highly improbable that any nutritional essential was entirely lacking, though it is possible that one or more, including vitamin A or vitamin D, might have been present in less than optimum amounts. Both vitamin A and vitamin D are concerned in the process of ossification. Deficiency in vitamin D is characterized by failure of osteoid tissue to lay down or to hold calcium salts. In complete vitamin A deficiency in rats epiphysial activity and bone growth cease, growth being resumed on restoration of vitamin A to the diet.[18a] The Mellanbys[19] also showed the relation of this vitamin to teeth and related structures. The response of the children receiving cod liver oil would depend primarily, then, other factors being constant, on whether vitamins A and D had previously been supplied to them in optimal amounts. If either or both of these vitamins had been present in less than optimal amounts, an improvement in nutrition and a consequent increase in rate of bone growth might be expected as a result of the cod liver oil supplement, which added approximately 700 units of vitamin D and 4,500 of vitamin A. If both had been adequate, no difference between the two groups could be expected.

What are the results? When the data from the initial roentgenograms had been collected, it was apparent that nearly half the children were above and somewhat more than half were below the Carter norms for their age; a third were 10 per cent or more below. It should be noted here that the Carter norms were obtained from children of the University of Chicago Laboratory School, a favored socioeconomic group. Therefore it is probable that they represent what is desirable

18a. Hess, A. F.; McCann, G. F., and Pappenheimer, A. M.: Experimental Rickets in Rats, J. Biol. Chem. **47**:395, 1921. Wolbach, S. B., and Howe, P. R.: Vitamin A Deficiency, in Growth and Development of the Child: III. Nutrition, White House Conference on Child Health and Protection, New York, Century Company, 1932, pp. 178-180. Dawson, A. B.: A Historical Study of the Persisting Cartilage Plates in Retarded or Lapsed Epiphyseal Union in the Albino Rat, Anat. Rec. **43**:109, 1929.

19. Mellanby, E.: Nutrition and Disease: The Interaction of Clinical and Experimental Work, Edinburgh, Oliver & Boyd, 1934.

TABLE 2.—*Deviation from Carter Index for Age for All Children at Beginning and End of Study, with Changes During the Year in Relation to Mean Index for Age and Sex and in Relation to Expected Gains*

Pair No.	Subject	Sex	Carter Index at Beginning	Mean Index for Age	Deviation at Beginning		Carter Index at End	Mean Index for Age	Deviation at End		Change in Deviation from Mean for Age		Gain in Score for Year		Percentage of Expected Gain
					Points	Percentage			Points	Percentage	Points	Percentage	Actual	Expected	
19 Matched Children of Control Group															
1	Gl. B.	F	65	60	+ 5	+ 8	74	71	+ 3	+ 4	— 2	— 4	9	11	82
2	M. L. B.	F	32	37	— 5	—14	42	46	— 4	— 9	+ 1	+ 5	10	9	111
3	H. C.	F	65	71	— 6	— 9	78	81	— 3	— 4	+ 3	+ 5	13	10	130
4	N. C.	F	71	64	+ 7	+11	81	76	+ 5	+ 7	— 2	— 4	10	12	83
5	V. L. C.	F	44	41	+ 3	+ 7	52	51	+ 1	+ 2	— 2	— 5	8	10	80
6	D. F.	F	74	74	0	0	75	84	— 9	—11	— 9	—11	1	10	10
7	D. I.	F	76	70	+ 6	+ 9	83	81	+ 2	+ 3	— 4	— 6	7	11	64
8	M. R. L.	F	34	46	—12	—26	43	55	—12	—22	0	+ 4	9	9	100
9	V. S.	F	81	79	+ 2	+ 3	87	88	— 1	— 1	— 3	— 4	6	9	67
10	I. T.	F	55	49	+ 6	+12	67	58	+ 9	+16	+ 3	+ 4	12	9	133
11	C. C.	M	39	47	— 8	—17	47	56	— 9	—16	— 1	+ 1	8	9	89
12	A. C.	M	34	39	— 5	—13	42	47	— 5	—11	0	+ 2	8	8	100
13	R. D.	M	46	50	— 4	— 8	56	59	— 3	— 5	+ 1	+ 3	10	9	111
14	J. L.	M	54	46	+ 8	+17	56	55	+ 1	+ 2	— 7	—15	2	9	22
15	H. L.	M	51	48	+ 3	+ 6	60	56	+ 4	+ 7	+ 1	+ 1	9	8	113
16	N. P.	M	36	34	+ 2	+ 6	44	43	+ 1	+ 2	— 1	— 4	8	9	89
17	R. P.	M	31	32	— 1	— 3	38	39	— 1	— 3	0	0	7	7	100
18	C. R.	M	15	20	— 5	—25	22	26	— 4	—15	+ 1	+10	7	6	117
19	B. T.	M	25	39	—14	—36	29	47	—18	—38	— 4	— 2	4	8	50
Total				1,011	—18			1,119	—43		—25	—20	148	173	1,651
Average						—1.78				—3.84			7.8	9.1	86.9
Percentage of expected gain for group														85.6	
Children of Additional Control Group															
20	S. A.	M	54	51	+ 3	+ 6	63	59	+ 4	+ 7	+ 1	+ 1	9	8	113
21	D. B.	M	48	53	— 5	—10	59	62	— 3	— 5	+ 2	+ 5	11	9	122
22	J. I.	M	72	66	+ 6	+ 9	75	74	+ 1	+ 1	— 5	— 8	3	8	38
23	V. H.	F	26	24	+ 2	+ 8	29	31	— 2	— 7	— 4	—15	3	7	43
Total				1,205	—12			1,345	—43		—31	—37	174	205	1,967
Average						—0.91				—3.20			7.6	8.9	85.5
Percentage of expected gain for group														84.9	

19 Matched Children of Experimental Group															
1	Ma. W.	F	59	71	−12	−17	73	81	− 8	−10	+ 4	+ 7	14	10	140
2	N. A.	F	33	35	− 2	− 6	44	45	− 1	− 2	+ 1	+ 4	11	10	110
3	F. T.	F	63	78	−15	−19	76	87	−11	−13	+ 4	+ 6	13	9	144
4	D. R.	F	73	63	+10	+16	80	74	+ 6	+ 8	− 4	− 8	7	11	64
5	D. J. D.	F	37	53	−16	−30	46	62	−16	−26	0	+ 4	9	9	100
6	D. S.	F	74	61	+13	+21	84	71	+13	+19	0	+ 2	10	10	100
7	J. T.	F	76	81	− 5	− 6	83	89	− 6	− 7	− 1	− 1	7	8	88
8	B. M.	F	33	45	−12	−27	43	53	−10	−19	+ 2	+ 8	10	8	125
9	V. W.	F	82	80	+ 2	+ 3	88	89	− 1	− 1	− 3	− 4	6	9	67
10	D. M. S.	F	48	43	+ 5	+12	55	52	+ 3	+ 6	− 2	− 6	7	9	78
11	B. O.	M	39	63	−24	−38	50	71	−21	−30	+ 3	+ 8	11	8	138
12	W. W.	M	36	37	− 1	− 3	44	46	− 2	− 4	− 1	− 1	8	9	89
13	L. P.	M	49	44	+ 5	+11	61	52	+ 9	+17	+ 4	+ 6	12	8	150
14	L. D.	M	58	53	+ 5	+10	66	62	+ 4	+ 7	− 1	− 3	8	9	89
15	F. W. B.	M	40	44	− 4	− 9	46	52	− 6	−12	− 2	− 3	6	8	75
16	J. L.	M	43	39	+ 4	+10	51	47	+ 4	+ 9	0	− 1	8	8	100
17	B. H.	M	34	30	+ 4	+13	41	36	+ 5	+14	+ 1	+ 1	7	6	117
18	C. B.	M	20	25	− 5	−20	22	29	− 7	−24	− 2	− 4	2	4	50
19	M. W.	M	26	29	− 3	−10	33	33	0	0	+ 3	+10	7	4	175
Total				974	−51			1,131	−45		+ 6	+25	163	157	1,999
Average						−5.24				−3.98			8.6	8.3	105.2
Percentage of expected gain for group														103.8	
Additional Children of Experimental Group															
20	Jo. T.	M	15	19	− 4	−21	18	24	− 6	−25	− 2	− 4	3	5	60
21	L. A.	M	28	29	− 1	− 3	34	35	− 1	− 3	0	0	6	6	100
22	J. McP.	M	29	31	− 2	− 7	33	37	− 4	−11	− 2	− 4	4	6	67
23	J. M.	M	7	19	−12	−63	11	25	−14	−56	− 2	+ 7	4	6	67
24	Ja. T.	M	18	26	− 8	−31	21	31	−10	−32	− 2	− 1	3	5	60
25	R. W.	M	23	21	+ 2	+10	29	26	+ 3	+12	+ 1	+ 2	6	5	120
26	Gr. B.	F	84	80	+ 4	+ 5	93	89	+ 4	+ 5	0	0	9	9	100
27	E. C.	F	86	81	+ 5	+ 6	90	90	0	0	− 5	− 6	4	9	44
28	A. H.	F	46	49	− 3	− 6	53	58	− 5	− 9	− 2	− 3	7	9	78
29	E. R.	F	58	56	0	0	73	68	+ 5	+ 7	+ 5	+ 7	15	10	150
Total				1,387	−70			1,614	−73		− 3	+23	221	227	2,945
Average						−5.05				−4.52			7.7	7.8	101.6
Percentage of expected gain for group														97.8	

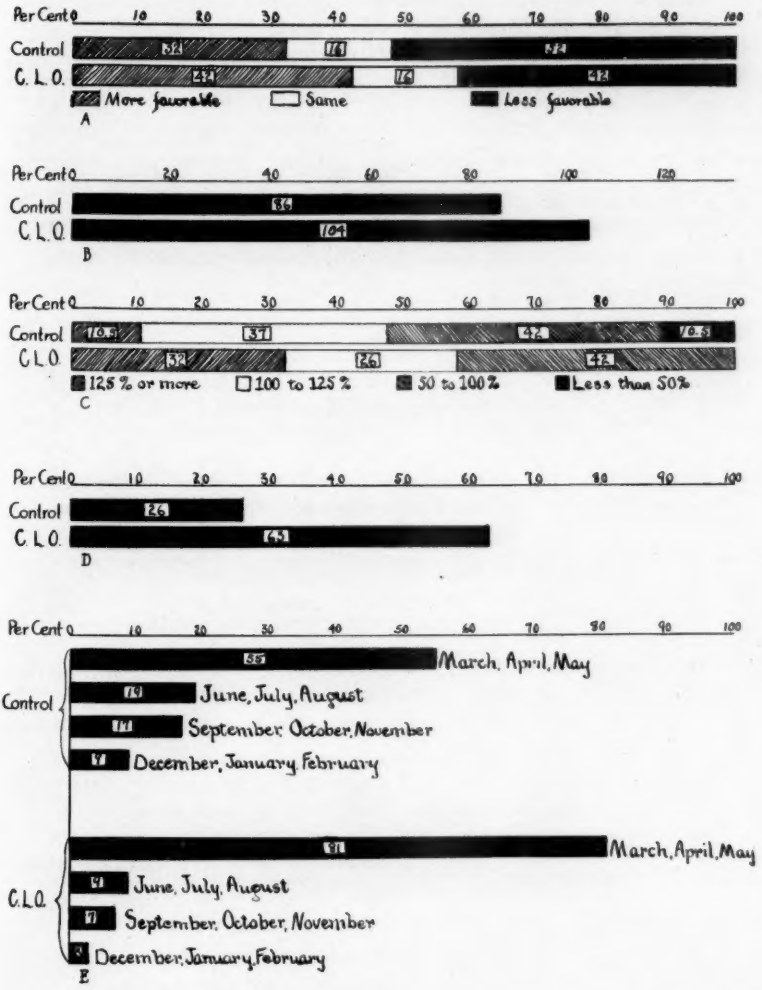
for all children rather than the actual average for all children or the average for those of the study. They are valuable as a means of comparison, however, because they have been obtained from a large number of children, 3,113, in a fairly stable group. With these norms as a basis of reference, the children of the study can be compared as to the relative amount of bone growth and the yearly gain in ossification. The relative status of each child, i. e., his deviation from the mean for his age, at the beginning and at the end of the study, was determined by comparing his initial and final ossification ratios with the Carter norms for his initial and final ages (table 2). The children whose ratios were 10 per cent or more below the means for their age would undoubtedly have been adjudged retarded by any standard taken from large numbers of average children. In both groups there were children who at the end of the year were still much below the average (table 3). In the control group the number retarded increased somewhat, from 47.5 to 57.5 per cent; in the group given cod liver oil the number retarded remained nearly the same, but here there was a slight shift of retarded children into a position of less retardation.

This change is shown more clearly by a consideration of the proportion of children in each group who improved their status or who lost in relation to the means for their ages. A child retarded at the beginning might still be retarded at the end of the year and yet might have made up a considerable amount of his deficit (table 4 and chart *A*). Of the control group 32 per cent, as compared with 42 per cent of the children given cod liver oil, were in a more favorable relation to the mean at the end of the year than at the beginning, while 52 per cent were in a less favorable relation, as compared with 42 per cent of the children given cod liver oil.

There are, however, more exact methods of showing differences in the year's growth of bone between the children who received the supplement and those who did not. These include three kinds of comparison: (1) of the matched groups, the control group and that taking cod liver oil, as wholes; (2) of proportions of the group in which advances of various sorts were made, and (3) of matched partners. The results are shown in table 2 and in the summaries given in tables 4 to 6.

In comparing the matched groups as samples of (1) children 3 to 10 years old receiving the institutional diet and (2) children of the same age receiving cod liver oil in addition, the pertinent figure is the percentage of the expected gain made by each group. In determining this figure the difference between the ossification ratio determined at the beginning and that noted at the end of the year represents a child's actual gain, and the difference between the norms for his initial and his final age represents the gain which might be expected of him. From these two values, the percentage relation of the actual gain to the expected gain can be computed for each child.

$\frac{\text{Actual gain} \times 100}{\text{Expected gain}}$ = Percentage of expected gain actually attained. It is possible also to total both the actual and the expected gains for all children in each of the two groups and thus to determine similarly the percentage of expected gain made by control and experimental groups



A, percentage of children in each group in more and in less favorable relation to the Carter mean for their age at the end than at the beginning of the year. "C.L.O." indicates the group given cod liver oil. *B*, percentage of the expected gain made by each group. *C*, percentage of children in each group making the gains specified, in percentage of the expected gain. *D*, percentage of the 19 pairs in which the specified partner made the best gain. *E*, proportion of the year's illness in each group for the specified quarter of the year.

when each is considered as a unit. Considering first the latter method of analysis, one finds (table 2 and chart *B*) that the control group made but 86 per cent of its expected gain in bone growth while the group taking cod liver oil made 104 per cent of its expected quota.

TABLE 3.—*Percentage of Children in Matched Groups Having the Specified Relation to the Mean at the Beginning and at the End of the Experimental Year*

Status	Control				Experimental			
	Beginning		End		Beginning		End	
	No.	%	No.	%	No.	%	No.	%
Even with mean or above	10	52.5	8	42	8	42	8	42
10% or more	3		1		7		3	
5 to 10%	5		2		0		4	
0 to 5%	2		5		1		1	
Below mean, less than 10%	3	16	5	26	4	21	4	21
1 to −5%	1		3		1		3	
−5 to −10%	2		2		3		1	
Below mean, 10% or more	6	31.5	6	31.5	7	37	7	37
to −15%	2		2		1		3	
−15% or more	4		4		6		4	
Totals	19	100	19	100	19	100	19	100

TABLE 4.—*Percentage of Children in Each Matched Group in More and in Less Favorable Relation to the Mean for Age at the End Than at the Beginning of the Experimental Year*

Status	Control Group		Cod Liver Oil Group	
	No.	%	No.	%
In more favorable relation	6	32	8	42
In same relation	3	16	3	16
In less favorable relation	10	52	8	42

TABLE 5.—*Percentage of Matched Children Making Specified Percentage of Expected Gains for the Year by Dietary Groups*

Amount of Gain, % of Expected Gain	Control Group		Cod Liver Oil Group	
	No.	%	No.	%
100 or more	9	47.5	11	58
125 or more	2	10.5	6	32
100 to 124	7	37.0	5	26
Less than 100	10	52.5	8	42
50 to 99	8	42.0	8	42
Less than 50	2	10.5	0	0

An analysis of the percentage of the expected gain made by the subjects in the two groups shows in children given cod liver oil the same tendency to excel (table 5, chart *C*). It is observed that the percentage of children making 100 per cent or more of their expected gains was greater in the group given a supplement than in the control group (58 per cent

versus 47.5 per cent). Moreover, fewer children in the group given cod liver oil made gains at the lowest levels and more children made gains at high levels than in the control group. Two of the control children made less than half the amount, and only 2, or 10.5 per cent of the group, made more than 125 per cent of the amount to be expected for their age, while in the group given cod liver oil none made less than half the expected gain and 6, or 32 per cent, made 125 per cent or more of their expected quota.

The most important comparison is that of the partners in the 19 pairs of children who were matched according to their skeletal development at the beginning of the study. As pointed out earlier, if the partners show like or nearly like development toward the mature pattern as judged by inspectional age, actual growth of bone as determined by the Carter ratio, and chronologic age, it is likely that they are in the same phase of growth. Direct comparison of partners is therefore the severest test of differences due to experimental procedure.

TABLE 6.—*Number of Times in Ninteen Matched Pairs the Specified Partner Made the Best Gain and the Amount of Superiority*

Partner Making Best Gain	Number of Times	Percentage	Excess, Carter Points	
			Total	Average
Control	5	26	14	2 8
Both the same	2	11	..	...
Cod liver oil	12	63	45	3.75
Difference in favor of partners given cod liver oil	..	..	31	1.63

From this standpoint, then, which of the partners made the best gains? Since the children were fairly well matched at the outset, the 2 children in each pair may be considered as having had an even start. If all conditions had been kept constant during the year, it might be expected either that the children in each pair would gain the same amount or that the higher gains would be about evenly distributed between the control and the experimental partners. If, however, the cod liver oil had an accelerating effect on development of bone and if this was the only variable introduced, the child in each pair having the supplement would presumably make the greater gain. The results of this method of analysis are given in table 6 and in the chart (*D*). It is at once evident that the best gains were by no means shared equally by the two groups but were predominantly attained by the partners receiving the cod liver oil supplement. In 5 of the 19 pairs the control child had better growth than his partner, while in 12 the child given cod liver oil did better than his control partner; in 2 pairs the partners made the same gain; i. e., the control partner excelled in 26 per cent and the experimental partner in 63 per cent of the comparisons. The fact that

not every experimental child outdistanced his control partner is not surprising, for other variables—especially illness, variations in consumption of food and absences from the institution—obscured the results. The amount of the difference between the partners and its statistical significance are important. The mean mathematical difference between the partners in the 19 pairs is $+ 1.63 \pm 0.55$ in favor of the partner receiving cod liver oil. This difference divided by its probable error is 3. This indicates that the difference may be significant, and not due to chance. This comparison of partners is the most direct and significant comparison of the progress of the two groups which can be made.

Thus in various kinds of comparisons of matched groups and matched partners the children given cod liver oil showed superiority, not large in any case but probably significant in the comparison of matched part-

TABLE 7.—*Progress in Osseous Growth of the Sixty-Seven Children of the Study During the Experimental Year*

Item	Control	Cod Liver Oil
Number of children	30	37
Percentage of children even with mean or above:		
Beginning	53	38
End	40	38
Percentage of children in more favorable relation to mean by 5% or more	13	22
Percentage of children in less favorable relation to mean by 5% or more	30	14
Percentage of expected gain attained	81	96
Percentage of children making expected gain or more	40	46
Less than 50%	17	8
125% or more	7	22
150% or more	0	11

ners. However, neither their size nor their statistical significance makes these differences between experimental and control groups important so much as the fact that they are consistently in the same direction, in favor of the children receiving cod liver oil. Therefore it seems that they can reasonably be ascribed to the experimental procedure.

The data from the study of the matched partners have been emphasized because they constitute a more precise measure of the experimental differences than do those from the study of the larger groups, but the data on the entire group of 67 (30 control children and 37 children given cod liver oil) are of interest. These are summarized in table 7. The table shows that, as in the 19 matched pairs, the experimental children advanced somewhat more than the controls. The percentage of those even with or above the norm remained the same in the group given a supplement, while in the control group it decreased from 53 to 40; 22 per cent of the children who had cod liver oil were in a more favorable relation to the mean for their age, by 5 per cent or

more, as compared with 13 per cent of the control children. The control group as a unit gained 81 and the experimental 96 per cent of the expected gain. Moreover, 17 per cent of the control children gained less than half the amount to be expected, and none made really large gains; 8 and 11 per cent are the respective figures for the group who took cod liver oil. Briefly, the evidence from the larger groups confirms that from the matched groups.

In connection with the significance of these differences there are two contributing factors to consider. First, at the home where the 19 pairs lived it is the custom to give cod liver oil for a week or two to any child who has had fever or a more serious disease, such as measles, scarlet fever or pneumonia. Sometimes, instead of the cod liver oil, a preparation containing cod liver oil, vitamin B complex and iron may be given. This procedure was not changed because of the experimental work. In this way 8 of the control children received a supplement of this kind for a week or so, the duration of the addition being as little as a week in most cases and as much as twenty-nine days in 1 case. An equal number of the experimental group were given some addition; i. e., the preparation of cod liver oil, vitamin B complex and iron was substituted for plain cod liver oil for periods similar in length to those of additions in the control group. In 2 cases an iron preparation was added, and in 1 case a vitamin C preparation was given for a week and then daily orange juice with the cod liver oil for a time.

Another custom of this home, as of most institutions of this sort, is to send children with any of the more serious contagious diseases to one of the Chicago hospitals equipped to take care of such patients. As a result, some of the children were away a month or more, and during their stay at the hospital the administration of cod liver oil was discontinued. Eight of the children who were taking cod liver oil had interruptions of this sort, and so the periods for the administration of the oil varied instead of being a full year for each experimental child as originally intended.

Second, among the variables which can be isolated and examined to some purpose are the duration and the severity of illnesses. Immediately after the first roentgenograms had been taken and the children had been divided into two groups which were matched as to skeletal maturity, there was an epidemic of children's diseases. In 1935 these diseases were rather more prevalent over the country than usual. Even among this comparatively well cared for group there were scarlet fever, measles, whooping cough, diphtheria (several cases) and pneumonia (several cases). As chance would have it, the larger number of these illnesses and of the more serious involvements occurred among the children given

cod liver oil. The administration of the cod liver oil was interrupted, or rather postponed, because the absences at the hospital all came at the beginning of the year. Moreover, it is doubtful whether those away from the home obtained as good food; in addition, it is rather generally accepted that illnesses of this sort and the accompanying fevers affect all growth and definitely retard development of bone. Stettner [8] (quoted from Flory [13]) found that "illness caused a cessation in growth and differentiation of the bony framework, the amount of the delay depending on the severity of the disease." In table 8 and in the chart (*E*) are indicated the duration and seriousness of the illnesses in the two matched groups; also, the proportion of the days of illness in each quarter of the experimental year. Several points are to be noted. The total number of days was much larger for the experimental than for the control group, four hundred and twenty as contrasted with two hundred and twenty-seven. The duration of the more serious contagious diseases amounted to two hundred and seventy days for the group given cod liver oil as compared with one hundred and seven for the control group. For both groups a larger portion fell in the first quarter, but again there was more illness for the children taking a supplement, 81 per cent of whose days of illness occurred in March, April and May, as against 54 per cent for the group with the nonsupplemented diet. Table 8 does not show that all the more serious diseases of the group given a supplement occurred during these months, in the first quarter of the year. Illness in the last three quarters included chickenpox, German measles and other mild disorders.

What might be expected under these circumstances? First, if Pryor, Rotch, Stettner, Todd and others were correct in stating that these diseases are nutritional disasters which affect ossification, the bone growth of the group taking cod liver oil might be much more retarded than that of the control group. All 19 experimental subjects had some children's disease, although a few escaped with nothing more serious than chickenpox or German measles. Second, some workers have expressed the belief that vitamin A specifically protects against disease and the damage that may result from it. What seems to be the total result in this case? The first noteworthy fact is that the group given cod liver oil had but 19 per cent of their illness after the first quarter while the control group had 45 per cent. This appears to be evidence for protection by the vitamins. Whether or not the cod liver oil was responsible for the decrease in illness in the experimental group, the second significant fact seems to be that, serious illness notwithstanding, the partners who had the supplement made a definitely larger advance in growth of bone than the control partners, who had less illness. It appears possible that the cod liver oil protected the experimental group from permanent

TABLE 8.—*Number of Children in Each Group Who Were Ill, Number of Days of Illness and Distribution of Illness over the Year, with Indication of Its Seriousness*

Group	Total Number of Children	Children Ill		Total Days of Illness	Days of Illness by Quarter Year								Days of Illness			
					1 March April May		2 June July August		3 September October November		4 December January February		Diphtheria, Scarlet Fever, Pneumonia		Measles, Whooping Cough	
		No.	%		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Control.....	19	16	84	277	153	55	52	19	48	17	24	9	69	25	38	14
Cod liver oil..	19	19	100	420	339	81	39	9	28	7	14	3	183	44	87	21

injury and allowed it, in spite of what might have been nutritional disasters, to make somewhat more than an average gain in bone growth and thus to make up a little of its deficit. The control group, on the other hand, increased its deficit, although it had much less severe and extended illnesses. It seems possible that the two vitamins were a protection for the process of ossification and prevented delay that might have been serious.

COMMENT

It appears that the good diet in this institution was susceptible of improvement. An increase in the amount of vitamins A and D seemed to allow for somewhat better growth of bone than the diet without the increase, and this improvement took place despite the greater duration and severity of the illnesses which the children with cod liver oil had to endure as compared with those of the control children. The diseases concerned—scarlet fever, measles, diphtheria and whooping cough—with their accompanying fever and occasional consequent pneumonia, are known to affect adversely both quality and rate of bone development. Improvement in the ossification of the group given a supplement was accompanied by a greater decrease in the incidence of illness than was noted in the control group for the last three quarters of the year. This may be another indication of improved nutritional status coincident with the superior bone development and related to the supplement.

Two particularly appropriate studies have been reported in which well children have responded to increased amounts of the dietary essentials employed in this study. The cod liver oil increased the amount of vitamins A and D in a diet which, as it contained some of all foods recommended for children's diets, was not known to be deficient in these vitamins. In the case of both vitamin A and vitamin D, however, it has been shown that "well subjects," children who to all outward appearances are in good health, may respond to increased amounts. Blunt and Cowan [20] mentioned the fact that more calcium and phosphorus are stored by an infant or young animal given cod liver oil or ultraviolet irradiation than by an untreated companion and that this phenomenon has been noted in well subjects as well as in those with rickets. Sherman cited the findings of Widmark and Svensson,[21] who gave vitamin A in the form of cod liver oil to children of school age in Malmö, Sweden. Although they found no appreciable difference between control and experimental

20. Blunt, K., and Cowan, R.: Ultraviolet Light and Vitamin D in Nutrition. Chicago, University of Chicago Press, 1930.

21. Widmark, E. M. P.: Vitamin A Deficiency in Denmark and Its Results, Lancet **1**:1206, 1924. Widmark, E. M. P., and Svensson, B.: Studien über den Bedarf und zur Verfügung stehende Mengen an fettlöslichen Vitaminen der Kinder in den Volksschulen zu Malmö, Skandinav. Arch. f. Physiol. **54**:127. 1928: cited by Sherman.[2]

children in height, weight, hemoglobin content of blood or evidence of night blindness, there was general improvement in health and vitality. Whether or not there had been a noticeable deficit, then, in this institutional diet, increased amounts of these two vitamins might approach the optimum and have a beneficial effect on nutrition and on development of bone.

It has been shown that almost any factor which influences the general nutritional condition has its effect on growth of bone as on all other tissues, though some essentials, such as calcium, may have a more specific function in relation to bone and therefore may have a more prompt effect than others which are less specific, such as energy. Rate of growth is undoubtedly proportional to many factors. Winters, Smith and Mendel [22] retarded growth in rats in various ways, with low calory, low protein, low lysine and low salt diets. The greatest modification of the dry weight of the bones took place in the group given a low salt diet and the least in the group given a low energy diet. Smith [23] in his review mentioned the persistence of the growth of bone in all these kinds of retardation of body growth. He referred also to the acceleration noted by Osborne and Mendel when animals were fed an adequate diet after having been stunted for a considerable time by various diets, which were low in protein, lysine, calories or vitamins.

As might be expected, therefore, in 73 children of the previously reported study [1] who received milk and in 37 of the study reported here who received cod liver oil in addition to their regular diet, there was appreciable modification of rate of skeletal development as compared with that of 65 control children. Before further discussion of results it is important to present in combined form the data from the studies on milk and cod liver oil. Comparison may now be made between all of the 110 children of both studies given a supplement and all of the 65 children not given a supplement (table 9). The gains in bone growth made by the children receiving an addition of milk or of cod liver oil to their regular institutional diet are seen to be definitely larger than those made by the children receiving the institutional diet alone. This superiority in growth was shown by every method used in comparing the groups. More than half the children receiving a supplement made their expected gain or more. Twenty-one per cent of them made 150 per cent or more of the gain indicated for their age by the norms. Considerably less than half the control children, 36 per cent, made the average gain or more, and of the 36 per cent only 5 per cent had large gains. Conversely, the larger losses were 10 and 18 per cent for the experimental

22. Winters, J.; Smith, A. H., and Mendel, L. B.: The Effects of Dietary Deficiencies on the Growth of Certain Body Organs, Am. J. Physiol. **8**:576, 1927.

23. Smith, A. H.: Phenomena of Retarded Growth, J. Nutrition **4**:427, 1931.

and the control groups, respectively. Forty-two per cent of the children given a supplement were in a more favorable relation to the mean for their age than at the beginning of the year as against 27 per cent of those without supplement. The larger number of the large gains (5 or more points) were made by the experimental group, 14.5 per cent, in contrast to 5 per cent for the control group, and the larger number of large losses by the control group, 20 per cent, in contrast to 7 per cent for the experimental group. The control children as a group made 85

TABLE 9.—*Progress in Bone Growth of the One Hundred and Eight Children of the Study on Milk, and of the Sixty-Seven Children of the Study on Cod Liver Oil*

Item	Control Group	Experimental Group
Number of children	65	110
Percentage of children even with or above mean:		
Beginning	29	26
End	23	26
Percentage of children 10% or more below mean:		
Beginning	46	46
End	47.7	41
Percentage of children in more favorable relation to mean by 5% or more	17	29
Percentage of children in less favorable relation to mean by 5% or more	23	11
Percentage of expected gain	85 ± 3.83	113.0 ± 4.18
Percentage of children making expected gain or more	36	54.5
Less than 50%	18	10
150% or more	5	22

TABLE 10.—*Statistical Summary: Comparison of Partners*

Set of Partners Compared	Pairs	Mean of Differences Between Partners	Difference / Probable Error	Probability of Difference Being Due to Supplement
Partners receiving milk				
Plain vs. control	24	2.71 ± 0.84	3.2	33 to 1
D milk vs. control	24	2.67 ± 0.77	3.5	55 to 1
Plain vs. D milk	24	0.04 ± 0.90	...	.....
Partners receiving cod liver oil				
Cod liver oil vs. control	19	1.63 ± 0.55	3.0	23 to 1
All partners receiving milk or cod liver oil				
Experimental vs. control	67	2.37 ± 0.44	5.4	3,000 to 1

per cent of the total gain in ossification to be expected, and the children given milk and cod liver oil, 113 per cent of their quota. The difference between these figures (28 ± 5.7) is statistically significant. The difference divided by its probable error is 4.9, which means that the chances are about 1,000 to 1 that the difference is not due to chance (table 11).

There is a further, more precise, comparison to be made, which concerns the 67 sets of partners (table 10). It will be seen here that the average difference between partners in these 67 sets is 2.37 ± 0.44; the difference divided by its probable error is 5.4. This indicates that

TABLE 11.—*Statistical Summary: Comparison of All Groups in Studies on Cod Liver Oil and Milk as to Percentages of Expected Gain*

Groups Compared	No. in Control Group	No. in Experimental Group	M_1	M_2	P. E. of $M_1 - M_2$	Diff. / P. E.	Probability Difference Is Not Due to Chance
Cod liver oil vs. control group							
Matched groups	19	19	105.2 ± 5.02	86.9 ± 4.99	18.3 ± 7.08	2.6	13 to 1
All children in larger home	23	29	101.6 ± 4.20	85.5 ± 4.72	16.1 ± 6.32	2.5	12.5 to 1
All children given cod liver oil	30	37	95.8 ± 3.98	80.7 ± 3.96	15.1 ± 5.61	2.7	14.6 to 1
Milk Groups							
Matched							
Plain vs. control	24	24	124.0 ± 10.6	78.0 ± 6.3	46.0 ± 12.4	3.7	79 to 1
D milk vs. control	24	24	118.0 ± 8.4	78.0 ± 6.3	40.0 ± 10.5	3.8	96 to 1
Plain vs. D milk	24	24	124.0 ± 10.6	118.0 ± 8.4	6.0 ± 13.5	0.4	.....
Total							
Plain vs. control	35	37	128.0 ± 8.96	87.5 ± 6.40	40.5 ± 11.0	3.7	79 to 1
D milk vs. control	35	36	120.3 ± 7.67	87.5 ± 6.40	32.8 ± 10.0	3.3	38 to 1
Plain vs. D milk	37	36	128.0 ± 8.96	120.3 ± 7.67	7.7 ± 12.0	0.6	.....
All subjects given milk or cod liver oil	65	110	113.0 ± 4.18	85.0 ± 3.83	28.0 ± 5.67	4.9	1,111 to 1

the chances are 3,000 to 1 that this difference is not due to chance and therefore that it may reasonably be ascribed to the experimental procedure.

The data from both studies seem to point to a definite relation between the increase in rate of bone growth and the improvement of the diets by the supplements. A greater change in rate occurred in the case of milk, which removed a larger deficiency, and a smaller change, as might be expected, in the case of cod liver oil, which was added to a diet with no great deficiency.. In each case there is reason to believe the results significant, because they are consistently in favor of the groups given a supplement. When the data from the two studies are combined, each set fortifies the other, and the two give definitely significant results. The study as a whole, then, yields data supporting the impression of a number of workers in this field that nutrition directly influences bone growth and that it does so quantitatively as well as qualitatively.

SUMMARY

Roentgenograms of the right hands and forearms of 67 children were taken at the beginning and end of a calendar year, and the progress in development of bone, as indicated by changes in the Carter ossification ratio, was followed. Half of the children were kept on the institutional diet as controls; half were given in addition a daily dessertspoonful of cod liver oil. The most valuable comparisons are those made for 19 pairs, each made up of a control and an experimental partner, who were matched at the beginning for sex and stage of bone development.

By all methods of comparison the group given a supplement showed somewhat greater progress than did the control group. The differences were all in the same direction, in favor of the children taking cod liver oil, although in the first quarter of the experimental year this group had two hundred and seventy days of illness with the more serious childrens' diseases, which are known to affect quality and quantity of bone growth. The control group had one hundred and seven days of similar illness. Although approximately one third of each group were retarded in respect to the Carter norms and were still retarded at the end of the study, the group given a supplement reduced, and the group without a supplement somewhat increased, their deficits. This is shown by the following summary:

1. The percentage of children in more favorable relation to the Carter standard for age at the end than at the beginning of the year was 32 for the control group and 42 for that given cod liver oil.

2. The control group as a whole gained 86 per cent and the group taking cod liver oil 104 per cent of its expected quota.

3. In the control group 47.5 per cent of the children gained the amount to be expected of them or more, while in the group given cod liver oil 58 per cent made such a gain.

4. In the 19 pairs the control child made the best gain in 5 (26 per cent) and the child receiving cod liver oil in 12 (63 per cent) of the comparisons. The amount of the superiority is shown in a comparison of the partners in the pairs as to variation from expected gain, the most accurate test of the result. By this method the mean advantage of the children in the group taking cod liver oil over their control partners was found to be 1.63 ± 0.55 points. As the relation of this difference to its probable error is 3, the advantage is probably significant.

5. The addition of a dessertspoonful of cod liver oil to an institutional diet every day for eight to twelve months of a year seemed to be a factor of safety and may have been a protection for the process of bone growth. This institutional diet, good as it appeared to be, was apparently susceptible of improvement.

When data from studies on both milk and cod liver oil are combined and the growth of bone of 110 children who were receiving a supplement is compared with that of 65 children who were not, the contrast between the groups is increased. The percentage of children in a more favorable relation to the Carter norm for age at the end than at the beginning is 27 for the group without the supplement and 42 for the group with it; the control group as a unit gained 85 per cent and the experimental group 113 per cent of its expected quota; in the control group 36 and in the experimental group 55 per cent of the children gained 100 per cent or more of the amount to be expected of them. In the 67 comparisons of matched partners the mean superiority of children given a supplement over their partners, who had none, was 2.37 ± 0.44. This difference is significant, as its relation to its probable error is 5.4.

Evidence has been presented to show that the rate of bone development in the wrist is related to the diet of the child. Supplements to institutional diets, a daily pint of reconstituted evaporated milk or a dessertspoonful of cod liver oil, have seemed to be a protection for the process of bone growth, for the children who were receiving them made somewhat better gains than those who were not.

Prof. Frank N. Freeman, of the Department of Education, University of Chicago, made available facilities for studying the roentgenograms, and Dr. Charles D. Flory and Dr. E. C. Bolmeier of the same department gave help and criticism. The Ritter Dental Company, through Mr. J. M. Dickinson, loaned the roentgen apparatus.

Dr. Lydia J. Roberts followed the study with guiding interest.

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HYPERPYREXIA FOLLOWING OPERATION FOR CLEFT LIP OR PALATE

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Hyperpyrexia following operation for closure of cleft lip or palate is so nearly constant, so alarmingly high, so prompt in its appearance and so unlike sequelae from operations at other sites that its presence constitutes a substantial challenge to those who prepare and to those who operate on patients with these conditions. Padgett [1] stated that a temperature of 103 F. or even 104 F. is almost to be considered normal the first afternoon after the operation in babies from 10 to 20 months of age, but that it should subside within twenty-four to forty-eight hours to 102 or 101 F. or less, or else all is not likely to be well. Seemingly there are two sharply defined varieties of hyperpyrexia: the immediate, which begins within a few hours after operation, and the deferred, which occurs a few days after operation. The latter type is like that which accompanies the usual postoperative infection, which requires a few days' time for incubation of an infective agent introduced or activated at the time of operation. The immediate type depends on factors to be discussed in detail later. The deferred type may continue with the immediate in some instances. The immediate type may subside in one or two days with no sequelae, or it may terminate in death within twenty-four hours. In the hope that a detailed study might throw some light on the causation and prevention of hyperpyrexia in such cases, we collected and tabulated from three services data on the last 100 serial operations. Only 12 per cent of the patients had a postoperative temperature of 100 F. or less.

Of the 100 consecutive operations performed from 1933 to 1937, 71 were for correction of cleft palate and 29 for correction of harelip. The operations were performed on 73 persons. Since some of the

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1. Padgett, E. C.: Surgical Diseases of the Mouth and Jaws, Philadelphia, W. B. Saunders Company, 1938, p. 1440.

73 patients were subjected to two operations, for statistical purposes the series will be considered to consist of 100 patients, unless otherwise indicated. For purposes of study, the 100 patients were divided into eight groups according to age (table 1). The average maximum postoperative temperature for each group, with the total duration of temperature, is shown in table 2.

TABLE 1.—*Classification of Patients with Cleft Palate and with Harelip According to Age Incidence* *

Age	No. of Patients	Operations for Harelip	Operations for Cleft Palate
Group 1, birth to 1 mo.	9	5	4
Group 2, 1 to 3 mo.	13	5	8
Group 3, 3 to 6 mo.	19	7	12
Group 4, 6 to 12 mo.	11	2	9
Group 5, 1 to 2 yr.	14	0	14
Group 6, 2 to 3 yr.	12	2	10
Group 7, 3 to 4 yr.	12	4	8
Group 8, 4 to 10 yr.	10	4	6

TABLE 2.—*Average Maximum Postoperative Temperature for Each Group*

Group	Patients with Harelip		Patients with Cleft Palate	
	Average Maximum Temperature, F.	Duration in Hr.	Average Maximum Temperature, F.	Duration in Hr.
1	101.2	24	101.9	25
2	101.9	31	102.6	41
3	103.1	33	102.6	64
4	101.4	62	103.9	67
5	.....	..	102.8	65
6	101.5	14	102.1	46
7	100.0	6	101.3	45
8	99.0	4	100.2	6

As indicated by the average for all the persons in a group, it was found that the temperature was lowest after operations for harelip in group 1 (under 1 month), continued slightly higher in groups 2 (1 to 3 months), 7 (3 to 4 years) and 8 (4 to 10 years) and was highest (over 103 F.) in group 3 (3 to 6 months). The temperatures of the groups with cleft palate, although nearly always higher, showed about the same variation, except for group 4 (6 to 12 months), which showed the highest of all groups, with an average maximum tempera-

ture of 103.9 F. for 9 patients. The duration in hours was, for the most part, longest for those groups having the highest temperatures.

EFFECT OF SIGNIFICANT FACTORS

Age.—In general, it will be noted that fever occurred to a lesser degree in the groups of patients under 3 months of age and from 4 to 10 years of age, while the highest temperatures were found in the group from 3 to 12 months of age, with slight drops until the patients reach their fourth year.

TABLE 3.—*Average of Highest Temperatures from 1933 to 1937*

Year	No. of Patients	Average Temperature, F.	Average Duration in Hr.	Year	No. of Patients	Average Temperature, F.	Average Duration in Hr.
1933	15	101.2	38	1935	32	102.0	42
1934	23	101.8	37	1936	30	102.8	48

TABLE 4.—*Temperature According to Seasons*

Season	Patients with Harelip	Patients with Cleft Palate	Average Maximum Temperature, F.	Average Duration in Hr.
Winter	4	17	101.9	46
Spring	11	23	102.2	50
Summer	6	13	101.8	23
Fall	8	18	102.0	47

Site.—Temperature in relation to the site of operation showed that the average postoperative temperature for patients with harelip was 101.4 F., and for those with cleft palate it was 102.2 F.

Year.—It is a well known fact that virulence of infection varies from year to year; table 3 shows mildly increasing variation in the four years tabulated.

Season.—Temperature in relation to the month and season of operation shows small variations, being slightly less in summer. The duration of fever averaged much less in summer (table 4).

POSTOPERATIVE COMPLICATIONS

Forty-one of the patients suffered from 51 postoperative complications, and of these the most common complications were those arising

from local reactions or from infections of the respiratory tract. They are tabulated as follows:

Local reactions	10
(Including 2 total sloughs of sutures; histories not accurate as to local reactions)	
Infections of the respiratory tract	21
Bronchopneumonia	11
Purulent rhinitis	3
Infection of the upper part of the respiratory tract, possibly rhinitis	3
Empyema	1
Otitis media	2
Tracheobronchitis	1
Disturbances of the gastrointestinal tract	2
Vomiting	1
Diarrhea	1
Involvement of the thorax	4
Dyspnea	2
Enlargement of the thymus gland	2
Dehydration	4
Miscellaneous	10
Anemia	2
Scarlet fever or rash	3
Impetigo	1
Eczema	1
Loss of weight	1
Albuminuria	1
Vaginal gonorrhea	1

There were complications in 7 cases of harelip, with 2 local reactions and only 1 infection of the respiratory tract. There were 44 complications after 34 operations for cleft palate on 14 persons, with 8 local reactions and 20 infections of the respiratory tract.

PREPARATION

Preparation for these operations varied in many particulars, but in general we now regard it as essential that the child should be in good health, as judged by freedom from fever for at least seven days previous to operation, as well as by freedom from anemia, contagious disease, infection and dehydration. We also consider it essential that the child be gaining weight. Some violation of these requirements occurred with untoward results, some of which will be cited later.

The best results were obtained when the child was placed in strict isolation with complete aseptic technic. The best safeguards against ever present infections of the upper part of the respiratory tract and their sequelae were isolation in a private room or cubicle with a private nurse. Visitors should be restricted to a minimum and then admitted

only when wearing masks and gowns. For patients who have had an infection of the upper part of the respiratory tract, at least four days' observation and a precautionary intramuscular injection of 15 cc. of parental whole blood should be ordered before operation. Hemoglobin of less than 70 per cent is an indication for active hematinic therapy until that percentage is reached. Wassermann, Kahn and urinary tests should be routine. Dehydration is best met by full oral intake of fluids until four hours preceding operation; immediately after operation subcutaneous injection of 5 per cent dextrose in Hartmann's solution should be started and continued until full oral intake is established. Preliminary typing of the blood is time saving when a postoperative transfusion is indicated.

Preoperatively, gains in weight are often difficult to attain because of the mechanical obstacles in feeding and also because of the decided susceptibility of these children to repeated infections of the upper part of the respiratory tract with parenteric diarrhea. Feeding programs should be founded on the fullest caloric intake tolerable, exactly proportioned, with all vitamins added. When needed, special feeding appliances and technic must be used. A prolonged period of delay is inevitable in many children before satisfactory gain is obtained, because many of the infants are marantic before admission.

The time spent in the hospital reflects the rapidity with which these preparatory steps were done:

Average total time in hospital for 100 patients..... 24.9 days
Average time in hospital before operation..... 9.2 days
Average time in hospital after operation..... 15.7 days
No. of patients in hospital over 7 days preoperatively..... 41
Total preoperative days, 791; average, 19 days
Total postoperative days, 683; average, 16½ days

While these precautions seemed adequate to us, it is worth noting that the elimination of a possible enlargement of the thymus gland is deemed of sufficient importance by Beatty [2] to warrant routine roentgen examination and treatment when indicated. He also advised routine medication with atropine preoperatively, a procedure which in our cases was followed by a very high temperature.

Preliminary examination by an otorhinologist for latent or chronic infection of the nasal or aural cavities was stressed by Padgett.[3] It seems worth while. He also expressed the belief that loss of much more blood occurs than is immediately evident, and he attributed certain ill after-effects to failure to compensate for this loss by immediate transfusion.

2. Beatty, H. G.: The Care of Cleft Palate Patients, Laryngoscope **46**:203 (March) 1936.

3. Padgett,[1] p. 1440.

The age at which the operation is performed bears an important relation to postoperative fever and sequelae. A unique and fundamental statement is that of Blair and Brown,[4] who wrote:

> The cleft lip is corrected . . . as soon as possible after birth. During the first few days of life there probably remains some of the immunity to surgical shock which is necessarily present during the process of birth. Operation may be done in the first twenty-four hours. In our series no deaths have occurred from operations on twenty-four-hour-old babies. . . . from the fourth to the tenth day, the clotting time may be prolonged and operation is not done in this period. . . . The occasional surgeon, however, had best wait until the fourth to the sixth month.

Our studies confirm their observations in that no deaths occurred in the group of patients under 3 months of age, and furthermore the febrile rise was much smaller in this group.

Of interest are the patients with postoperative temperatures of 104 F. and over who recovered. There were 10 patients, their ages being 5 weeks, 9 weeks, 3 months, 6 months, 10 months, 1 year, 1½ years, 1½ years, 2 years and 4 years. One had bilateral otitis with chronic discharge and after her two operations showed temperatures of 105 and 104.8 F. None of the other 9 had any observed preoperative pathologic condition or fever. Two had cleft lips, and 8 had cleft palates.

TREATMENT

In our efforts to prevent the occurrence of postoperative fever, we tried many measures in addition to those in the general plan already outlined. It is interesting to note in a study of the 10 recovered patients (19 cases) with a temperature over 104 F. that subcutaneous injection of fluid in both large and small amounts was futile in 5 cases. Intramuscular injection of blood was used in 3 of these cases. In the hope that antiallergic drugs might prove effective atropine was given in full dosage before and after operation in 5 cases, but this succeeded only in apparently making the fever greater. Epinephrine hydrochloride given in full dosage subcutaneously was also futile. Acetylsalicylic acid and phenobarbital preoperatively administered were useless as preventives. The duration of temperature was less than forty-eight hours in 14 cases and more than that in 5 cases, in 3 of which pneumonia was diagnosable.

Postoperatively, the treatment in 8 cases was subcutaneous administration of fluids; in 11 cases recovery was obtained with oral administration of fluids; whole blood injected intramuscularly was used once. Morphine was used in 6 cases and phenobarbital in 4 cases for sedation.

4. Blair, V. P., and Brown, J. B.: Diseases of the Mouth and Adnexa, in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1937, vol. 3, chap. 1, p. 3.

Isolation was only partially effected. It was possible to quarantine the infants from other infants but not fully from all adults, some of whom refused the isolation technic of mask and gown.

Seven of these 10 infants showed a temperature of more than 104 F. for both of their operations, despite all precautions. As the temperatures in the other 90 cases did not show this height, that fact seems to indicate a special predilection for reactions of high temperature in certain children. It seems nearly certain that a high temperature will follow the second operation if it has occurred after the first.

There were 3 deaths in this series of 100 operations. Brief accounts of these follow.

C. M., aged 3 months, was operated on in May 1933. He had low grade bilateral otitis media at the time of operation and died five days later from bronchopneumonia. Permission for autopsy was refused.

D. W., aged 4 months, was operated on in November 1935. He was admitted to the hospital at 9 p. m. showing a temperature of 100.6 F.; nevertheless he was operated on the next morning at 10 o'clock. He had a temperature of 104 F. four hours afterward, 106 F. seven hours afterward, and he died eighteen hours after the operation. Autopsy showed diffuse congestive tracheobronchitis and bronchopneumonia of the lower lobe of the left lung and of the upper and lower lobes of the right lung and cloudy swelling of the parenchymatous organs.

There was no pediatric or otolaryngologic consultation for D. W., and the period of observation was twelve hours. Temperatures over 99.8 F. rectally should be regarded as an indication for postponement until there have been several afebrile days.

J. C., aged 1 year, was operated on in October 1936 and died seven hours later. He had had a previous operation for harelip in April 1936, after which bronchopneumonia, otitis media and empyema developed; for which drainage by the open method was maintained for many weeks. After eighty-one days' hospitalization he was sent home for about three months, after which he returned to the hospital. After four days' observation, during which he was afebrile, he was operated on for cleft palate and died seven hours later. Autopsy showed diffuse bronchopneumonia in the stage of red hepatization.

Four deaths occurred before operation, all from bronchopneumonia. Three patients became ill within twenty-four hours after admission, 1 a week after admission. All were under 6 months of age, and all were admitted in 1933 and 1934.

ETIOLOGY

It seems plausible that the denudation of a relatively large area of tissue with subsequent sealing by sutures may provide atria for the sudden introduction directly into the blood stream of a large amount of transuded blood, of bacteria or of unknown biochemical toxins. These "foreign" proteins, substances or bacteria may stimulate reaction in tissues, especially in those tissues previously sensitized by infection. In the 2 postmortem examinations reported the discoverable pathologic

condition was that of the first stage of pneumonia and accords with the observations reported for fulminant pneumonia.

Possibly a lesser degree of similar tissue reaction not physically diagnosable is present in those patients who recover. It is a fact that of all cases of immediate hyperpyrexia which continued after forty-eight hours, diagnosable bronchitis and pneumonia were found in 11 per cent.

Evidence is presented in this study of a special tendency to the occurrence of high temperature in patients previously infected and in those having fever after a previous operation. Antiallergic drugs did not prevent this reaction. It is highly significant that this reaction was absent or very mild in 2 groups of patients, those under 3 months and those over 4 years. Possible explanation of these facts may lie in the existence of a physiologic defense mechanism, termed by Blair and Brown [4] "the immunity to surgical shock which is necessarily present during the process of birth." Is this immunity regained after the fourth year? Or could this early defense be due to placentally transferred antibodies which protect the child during the first months of life only to disappear thereafter until generated again at about the fourth year to prevent this reaction? Such immune reactions are more or less common with respect to many other infections in children. The plausibility of this view is strengthened by the evidence showing the absence of a relation to season, year or dehydration before or after operation, as well as by the negative effects of antipyretic and antiallergic drugs and the extent of hemorrhage.

The preventive effect of large transfusions given before operation was not tested, but in the 3 cases in which the patient received whole blood intramuscularly before operation, hyperpyrexia occurred. The quantity and protective titer of the blood may have been insufficient, or the immune bodies or the defense mechanism may reside in the tissues rather than in the blood.

SUMMARY

Our studies indicate that the significant constant factors involved in the causation of immediate hyperpyrexia following operations for cleft palate and for cleft lip are the age of the patient, the site and extent of the operation (greater in cases of cleft palate than in cases of cleft lip), the existence of previous or latent infections and high temperature following a previous primary operation. Secondary or deferred fever is less frequent when infection or contagion is prevented by isolation and observation for a period of at least seven days and when the patient is placed in the highest obtainable degree of general good health.

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DISCUSSION

DR. H. A. POTTS: Some time ago when Dr. Stepan asked me if I should object to his reviewing such cases as we might have observed at St. Luke's Hospital, I told him that I had studied the hyperpyrexia following this type of operation rather meagerly but had come to the conclusion that it was idiopathic and just one of the things that is going to happen. Thirty years ago Dr. Gilmer used to prescribe "a good stiff dose" of castor oil in all such cases but found that after a day or two the temperature would go down anyway, so he did not give castor oil any more. It seems to me from this report that present day physicians are not far ahead of that idea. They are going to have to deal with this idiopathic hyperpyrexia in spite of anything they can do. I do not remember a case of Dr. Gilmer's nor one of my own that was fatal. So I do not defer operation or refuse to operate because I am afraid that the patient will have a high fever afterward.

The other type of fever spoken of is due to some pathologic condition. Most of the patients are infected. I doubt very much whether the idiopathic hyperpyrexia is due to infection, but patients with the other type, as postmortem examination shows frequently, do have infections, especially of the respiratory tract. Thymic enlargement is not a new topic, but I can speak from the experience of having lost 2 patients with this condition. With the first patient my associates and I had taken roentgenograms and found an enlarged thymus. The patient received roentgen treatment and was supposedly normal. I operated, as always, on the lip and most of the anterior part first, successfully. There was an uninterrupted recovery from the first operation. The child came back in two or three months for the operation on the palate, and as roentgenograms of the thymus had been taken recently I did not think it was necessary to take roentgenograms, and I performed the operation. On the fourth day the child just faded away and died from shock. No stimulation had any effect; we even injected epinephrine hydrochloride into the heart muscle. Autopsy revealed status lymphaticus, with enlargement of the thymus. I had a similar experience about two months later. No roentgen pictures were taken. The child on the fourth day after operation went into increasing shock and died. Again autopsy showed status lymphaticus, with an enlarged thymus. Since then I have taken roentgen pictures of babies who are to be operated on for cleft lip or palate and if the thymus is enlarged the child receives roentgen treatment. Simply because enlargement of the thymus seems to be part of the lymphatic state, I feel that when I have had the child treated by roentgen rays I have done all I could, and that is my answer to that question.

I remember a child who before operation had a few spasms with stridor. This difficulty in respiration continued after operation, at times with a little stridor, but that was overcome, and the child recovered after a week or so of treatment with oxygen and carbon dioxide.

In our service children with this deformity are operated on at the earliest age possible. The earliest I have done the operation on the lip has been the third day. As soon as the child has recovered from the first operation and is in good health, I do the second operation. The season seems to me not to make a great deal of difference. Blair of St. Louis does all his work in the summer, and maybe that is wise. In all our cases the child is prepared for operation, and we are told when we can operate by the pediatrician. Many times I have appeared in the operating room ready to operate and have been informed that the child's temperature rose during the night to 99 and that operation is deferred. I do not operate without the consent of the pediatrician. I like to have the baby gain in weight, and to achieve this is his duty.

When there have been symptoms of shock, we inject 30 cc. of mother's blood subcutaneously or intramuscularly one to three hours after operation, but as a routine our babies get a coffee enema, are kept warm and are given a little oxygen and carbon dioxide. There is one other condition which I think should be a warning, and that is jaundice. Severe jaundice in the child should be an indication to defer operation.

I am very glad indeed that Drs. Irish and Stepan have made such a review and investigation. So far I am convinced that there is not much to do about the idiopathic type of hyperpyrexia. The other complications, I think, can be avoided by being sure there is no latent infection present at the time of operation.

DR. LOUIS SCHULTZ: At the Research and Educational Hospital, all cases are passed on in the pediatric department, the same as here at the Children's Memorial Hospital. But in spite of that protection we see such infections as scarlet fever, erysipelas, measles and chickenpox develop in patients even after the pediatricians have "gone over them with a fine tooth comb." However, so far we have encountered no lasting ill effects from these complications. I had one youngster with erysipelas in my service, and I thought I would not have a nose or a face on this child when I got through, but he surprised all of us. One patient requiring operation on the palate sent from the Research and Educational Hospital to the Cook County Hospital—no reflection on that hospital—did not fare so well.

My conviction is that dehydration plays an important role in patients suffering from hyperpyrexia preoperatively or postoperatively. I will operate on a child with a temperature of 99 or 100 F. if no rales, no cough or rash is present. If consumption of food is stopped four hours and that of water two hours before operation, a rise in temperature may be expected. So far I have been fortunate—the mortality rate is low—I dare say, between 1 and 2 per cent. Maybe that is too high. I think elevation of temperature is a direct reaction, an indication of the ability of that youngster to fight. Conversely, a child with infection and without a rise in temperature presents a poor risk. Physicians all recognize that. Early high temperature does not alarm me—103 or 104 F. for a day or two—but if it remains high I call on the pediatrician for help. Many of these children are in a state of malnutrition. That would be a poor start, but I ask the pediatrician to take care of that. When the babies are in proper shape, they may continue to gain postoperatively. Also, postoperatively I give all the fluid the child will take by mouth and more subcutaneously when needed. I find that with a solution of 5 per cent dextrose and 3 per cent sodium bicarbonate they get along nicely. Parental blood injected intramuscularly is of decided value for such children when they get into trouble.

With reference to seasonal operations, I know that some surgeons refrain from operating in the winter; I have not found this necessary; in fact, I would rather operate in the winter, because the operating room is not so warm. The babies fare just as well in my hands.

I must disagree with Dr. Potts, whom I hold in high esteem, with regard to the thymus. Some years ago I lost a couple of children who had enlargement of the thymus, and after that I took roentgenograms of babies with cleft lip or palate before operation, as a routine. But Dr. Brennemann questioned the necessity and said I was placing too much weight on the roentgen evidence of the state of the thymus, and again take fewer roentgenograms. If I can lessen delay, I do so always. If a child is suffering from respiratory embarrassment, I do not operate but have a routine examination of the thymus made.

Some palatal muscles have their origin at the pharyngeal opening of the eustachian tube. As long as children have cleft palate, they are prone to have otitis media, but if they have been afebrile for several weeks, I operate. My experience has been that these children fare well even if they have chronic infection of the ear.

As long as a sizable cleft of the hard palate is present, the child is prone to have a nasal discharge, but this is not an indication to postpone operation.

The time of operation, I hold, should be as early as possible after the third week, at which time a suitable diet may have been established.

I do not give preoperative medication. I feel I have enough to do if the infants happen to be affected adversely on the table and have had ether only. However, I start by giving them a few whiffs of ethyl chloride and then switch to ether.

DR. CHARLES K. STULIK: As a pediatric consultant on surgical intervention, I have been able to check 226 cases in which Dr. Moorehead has operated at the Presbyterian Hospital. We have a regular routine, including the administration of water up to one hour before operation. In the last two years we have had 4 patients with temperatures above 103 F., the average being about 101 F. The infant with harelip is operated on preferably when it is about 8 weeks of age, i. e., when its feeding has been stabilized and it is gaining weight and is free from infection.

With reference to thymic reaction, we had two deaths before we made routine roentgen examinations of the thymus. We give 5 to 15 minims (0.30 to 0.90 cc.) of camphorated tincture of opium U. S. P. as the babies come out of the anesthesia and find it is of value in controlling postoperative restlessness. The older children with cleft palate are often given small doses of codeine. At the American Hospital in Paris they think that the postoperative elevation of temperature in cases of operation about the head and neck might be due to stimulation or irritation of the pituitary, and small doses of epinephrine hydrochloride are injected before operation with apparent benefit. Several children who have been operated on repeatedly—some as many as six or eight times—had about the same temperature at each operation, so possibly these children have a defect in the heat-regulating apparatus. Preoperative transfusions have been of value in selected cases. Anesthesia and the danger of aspiration of serosanguineous material are watched carefully.

DR. CLIFFORD G. GRULEE: It has been rather a long time since I have taken any definite interest in the subject of cleft palate and harelip, but I did at one time. I had the impression at that time that the presence of enlargement of the thymus was more frequent in children with cleft palate than in the average run of children. Why that should be I do not know, or whether it is true I do not know. The question I want to raise is this: Why has every one taken for granted that enlargement of the thymus is dangerous? I do not know that it is. Pediatricians have no definite evidence that an enlarged thymus is a cause of death. They know that a child who dies suddenly may have an enlarged thymus, but that the enlargement of the thymus is responsible for the death they have no proof. I think patients with harelip and cleft palate have definitely enlarged thymuses because they are below par from a nutritional standpoint. If the nutrition is good and the thymus is large, I pay no attention to the thymus. If the nutrition is low and the thymus is large, I do pay attention.

My colleagues and I attended a child brought to the hospital with vomiting and other indications of a gastrointestinal upset. We decided to send this child to the roentgen laboratory to have a roentgen examination made of the bones. A roentgenogram of the chest was taken by mistake, and it showed a large area of thymus. That child had no symptoms and did not appear to be a lymphatic child at all. What is the significance of enlargement of the thymus? I do not know, and I think it is a mistake to regard it as dangerous until one is sure.

Dr. Potts advised against operating when the child is icteric. Yet every newborn child is potentially icteric because of the high bile salts in the blood. Is there any reason to use that as a contraindication to operation for harelip in a newborn infant?

DR. CHARLES E. STEPAN: I think that probably the most important factor from the point of view of the pediatrician is to see that patients of this type are afebrile for at least seven days. That means controlled temperature, whether the patients are at home or in the hospital. They should be in the hospital for a minimum length of time—four days. We consider any temperature over 100 F., taken rectally, as a fever. I should like to stress fluid intake. We have since this paper was written made sure that patients to be operated on for cleft lip and palate have adequate fluid intake up to four hours before operation and subcutaneous injections of fluid immediately afterward. We have cut complications to a minimum.

When to operate—any time in the first three months seems to be the most advantageous time. I was surprised, when I read these charts, to see the number of cases in which cleft lip and palate were operated on within forty-eight hours after birth. The results in these cases are truly spectacular. We had only 1 patient with a postoperative temperature of over 100 F. and none with postoperative complications. We thought the fever started only after operation, but it may start during operation. We have often found fever starting one-half to one hour after operation. We have found that an elevation of temperature may occur while the child is on the operating room table and are now working on that. So far as preoperative medication is concerned, nothing seems to help in reducing the incidence of the idiopathic type of temperature, but we have reduced the incidence of prolonged high temperature or of true infection of the respiratory tract by applying the rules of watching for preoperative fever and insuring an adequate intake of fluid.

Case Reports

CONGENITAL LEUKEMIA WITH "CHLOROMA"

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AND

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Congenital leukemia is rare. Since 1888 approximately 27 cases have been reported (table). In none of these was the condition definitely monocytic; in 7 it was lymphocytic and in the rest myeloid. The ages at which the patients were first encountered ranged from newborn (stillbirth) to 26 months. Nine patients were less than 1 month old when first observed. Of these, in only 7, in all probability, was the involvement truly congenital. Actually but 4 patients with congenital leukemia were followed from birth, if the 2 stillborn infants are excluded. These were the patients of Siefart, reported in 1898, and of Nobécourt, in 1905, the patient with leukemic myelosis reported by Swart in 1905 and also studied by Schridde and the one with acute leukemia reported by Chapman and Ewart in 1932. Despite these, Feer, Finkelstein and Naegeli have denied the occurrence of leukemia in the newborn. This view has been opposed by Baar and Stransky and Opitz.

The case here described is reported not alone for its rarity but because a complete study was made during life, including biopsy of the skin, aspiration of sternal marrow, examination of the placenta and umbilical cord and complete autopsy. Furthermore, the results of these studies may shed some new light on the nature of congenital leukemia.

REPORT OF A CASE

An infant was delivered in the Jewish Hospital on Jan. 13, 1938, at 12:30 a. m. The mother, M. C., a 25 year old primipara, was a twin. Her menstrual periods began at the age of 14 and were irregular, with severe pains at the onset. Her last menstrual period began on March 28, 1937. Fetal movements were first felt in August. The woman was admitted to the hospital at 11 p. m. on Jan. 11, 1938, in the first stage of labor. On her admission the temperature was 98 F., the pulse rate 78, the respiratory rate 20 per minute and the blood pressure 132 mm. of mercury systolic and 80 mm. diastolic. The fetal heart was audible in the left lower quadrant of the abdomen. The first stage of labor lasted thirty-one hours

From the Division of Hematology of the medical and laboratory services of the Jewish Hospital.

and twenty minutes, the second stage, fifty minutes. Delivery was spontaneous. The presentation was cephalic, the occiput appearing to the left anteriorly. A normal placenta was expelled five minutes later.

At birth the baby had a pink skin and a lusty cry. There were no abnormalities of the eyes, ears, nose or mouth. The heart and lungs were normal. The abdomen was not distended. The liver and spleen were not palpable. The lymph nodes were not enlarged. The extremities and genitalia were normal. The reflexes were active. The spine was normal. The skin presented faint blue-violet flecks (fig. 1 *A*); these were infiltrative and irregular, measuring about 5 or 6 mm. in length and 2 or 3 mm. in width. They were not purpuric spots and were scattered over the whole body. Especially interesting and striking were three tumor-like masses (fig. 1 *B*), two on the back and one on the scalp. The lesion on the scalp was situated in the left parietal region, near the junction of the sagittal and coronal sutures. It was red and about 2 cm. in diameter; it felt somewhat cystic, though relatively firm, but was not adherent. To the right of the vertebral column at the level of the spine of the scapula was a violaceous tumefaction which looked like an ordinary contusion. It was about 3 cm. in diameter and was freely movable but not fluctuant. A similar tumefaction was present slightly above the

Fig. 1.—The patient shortly after birth. *A* shows the flecks on the skin; *B*, the tumor-like masses.

iliac crests; this was firm to the touch and somewhat fluctuant and at the surface apparently had a central area of necrosis 2 cm. in diameter.

The mother's Kline reaction was negative. The tumefactions slowly diminished in size. On the other hand, the widespread infiltrative flecks became more prominent and numerous. The bleeding tendency became more apparent at this time. The bleeding time was prolonged, and vaginal blood stains appeared. On January 19 a study of the bone marrow showed that myeloblasts and premyelocytes comprised 67 per cent of the cells, myelocytes 13 per cent, eosinophilic myelocytes 8 per cent, metamyelocytes 1 per cent, staff forms 2 per cent and polymorphonuclear leukocytes (lobocytes) 9 per cent. The granulocyte-lobocyte ratio was 91:9, granulocyte-erythroblast 90:10, early-late erythroblast 25:75 and myeloid cell–lymphocyte 85:15. Ten per cent of the myeloblasts were vacuolated; platelets and megakaryocytes were not seen.

In addition, studies of peripheral blood smears [1] showed many immature cells resembling atypical myeloblasts (Osgood cells 56 and 61, Osgood and Ashworth: Atlas of Hematology). The platelets were definitely diminished. The impression

1. Photomicrographs will be included in a pathologic review of this case.

was that of leukemic myeloblastosis with cutaneous manifestations or possibly leukemic monocytosis. On January 22 other firm blue nodules appeared in the skin. The infant continued to eat well and gain weight, and the temperature remained

TABLE 1.—*Reported Cases of Congenital Leukemia*

Report No.	Date of Report	Author	Age of Patient	Type
1	1888	Sänger	Stillborn	Lymphocytic
2	1898	Siefart	Few hours	Lymphocytic
3	1898	Pollmann	18 days	Myeloid
4	1904	Zuccòla	.....	Myeloid
5	1905	Larrabee	6 weeks	Lymphocytic
6	1905	Lommel	38 days	Lymphocytic
7	1905	Nobécourt	Newborn	.....
8	1905	Schridde and Swart	Newborn	Myeloid
9	1914	Vollenweider (4 cases questioned by Pappenheim)		
10	1921	Smith	6 weeks	Lymphocytic
11	1921	Ghon	6 months	Myeloid
12	1922	Koch (2 cases)	11 and 10 months	Myeloid
13	1924	Rupilius	.....	Myeloid
14	1924	Solmitz	15 months	Myeloid
15	1924	Bloch and Hirschfeld	8 months	Lymphocytic
16	1924	Benjamin and Sluka	13 months	Myeloid
17	1924	Caronia	26 months	Myeloid
18	1924	Opitz	3 months	Myeloid
19	1925	Stransky	3 weeks	Myeloid
20	1925	Malmberg	5 months	Myeloid
21	1930	Salomonsen	5 months	Myeloid
22	1931	Büngeler	Stillborn (7 months)	Myeloid
23	1932	Chapman and Ewart	Newborn	Lymphocytic
24	1934	Kornmann	6 weeks	Myeloid
25	1936	Lereboullet and Baize (several cases)		
26	1937	Saxl	8 months	Chloroma (leukemic myelocytoma)
26	1937	Saxl	4½ months	Myeloid
26	1937	Saxl	6 weeks	Myeloid
27	1937	Cooke	4 days	Lymphocytic

TABLE 2.—*Hematologic Data for the Patient and the Patient's Family*

Date	Subject	Hemoglobin, %	Red Cells, Million	White Cells, No. per Cu. Mm.	Myeloblasts, %	Myelocytes, %	Metamyelocytes, %	Eosinophilic Myelocytes, %	Staff Forms, %	Polymorphonuclears, %	Eosinophils, %	Lymphocytes, %	Monocytes, %	Platelets	Red Cells, Morphology
1/17/38	Infant	110	4.8	30,000	71	0	1	0	2	17	1	8	..	Diminished	0
1/18/38	Infant	...	...	.....	44	2	1	0	1	27	0	32	3	++	..
1/20/38	Infant	100	4.6	104,800	..	..	..	..	..	..	..	..	..	....	..
1/23/38	Infant	...	...	.....	66	..	..	..	..	..	8	26	..	....	..
1/25/38	Infant	...	...	300,000	..	..	..	..	..	..	..	..	..	....	..
1/25/38	Father	...	...	.....	..	..	..	..	2	58	2	34	4	+++	0
1/25/38	Mother's sister	...		.....	..	..		..	..	70	2	25	3	+++	0
1/25/38	Mother	...	...	.....	..	..	..	..	..	63	1	33	3	++	0
2/ 2/39*	Infant's sister (newborn)				..	..	..	..	..	71	3	20	6	++	..

* After this article was submitted for publication.

normal. On January 22 biopsy of a cutaneous nodule was made. The pathology department (Dr. D. M. Grayzel) reported that the lesion resembled leukemic infiltration. On January 23 numerous additional cutaneous nodules appeared. These were firm, hard and freely movable under the skin. A few pinpoint-sized hemorrhagic spots appeared on the neck and chin. The temperature rose to 100.8 F. On the following day the temperature had returned to normal. The liver

was definitely enlarged. The spleen was not palpable. Many more petechiae appeared on the face, neck and body. That afternoon there was a postnasal discharge, and the temperature rose to 102.6 F. The abdomen was distended. A large lymph node was palpated in the right axilla. The dermatologist (Dr. Jacob Skeer) diagnosed the lesions of the skin as leukemic. On January 25 the temperature rose to 103.4 F. The heart rate was rapid. The lungs were clear. The abdomen was distended. New petechiae appeared on the neck. The infant became listless, and the respirations became shallow. At 3:55 a. m. on January 26 the patient ceased breathing.

For the purpose of this report only a summary of the autopsy need be given. Macroscopically there was seen enlargement of the liver, spleen, pancreas, kidneys, adrenal, thyroid and thymus glands and lymph nodes. The external and the cut surfaces of all the organs presented petechiae. In addition there was a soft yellow-green irregular mass measuring 3.5 by 2.5 by 1 cm. in the left inguinal region, attached to the psoas muscle and the pelvic bone. Another mass, measuring 4 by 3 by 1 cm., was attached to the inferior surface of the diaphragm just lateral to the right adrenal gland and the upper pole of the kidney.

On microscopic study the May-Grünwald stain everywhere disclosed infiltrations of large mononuclear cells with large round or indented nuclei and abundant cytoplasm which reacted positively to the oxidase stain. These cells were often arranged in dense clusters in different organs. They were especially prominent in the spleen, liver, bone marrow, tumor masses, pancreas, kidneys, thymus, thyroid and adrenal glands, lymph nodes, heart, lungs, gastrointestinal, urinary and genital tracts, skin and diaphragm.

Remarkable is the fact that although there was observed only an occasional immature cell in the placenta and in the maternal and the fetal part of the cord at birth, clusters of this type of cell were abundantly present in the fetal end of the cord, at the abdominal wall, on postmortem observation.[2]

COMMENT

At birth the infant presented indefinite tumefactions of the back, associated with moderate leukocytosis which was assumed to be within normal postnatal limits. Possibilities in differential diagnosis of the tumefactions were fat necrosis, angioma neonatorum, spina bifida occulta, sarcoma, congenital syphilis and interpartum dystocia caused by pressure phenomena incident to intrauterine fibromas.

Since there was no enlargement of the liver, spleen or lymph nodes, since the hemoglobin content was 110 per cent (Sahli) and since no petechiae were present, a diagnosis of leukemia could not be entertained. However, a study of the peripheral blood showed the presence of 71 per cent large immature cells with round or indented nuclei. The latter were regarded at first as monoblastic but finally as myeloblastic.

2. Routine examination of the placenta and of the umbilical cord at birth revealed only an occasional cell. At autopsy these immature cells were seen in large numbers in the fetal end of the umbilical cord. For conclusions as to the presence of some substance in the umbilical cord which does not allow the cells to migrate into the placenta, routine sections through the fetal end of the umbilical cord would have been necessary.

Aspiration of the bone marrow of the sternum just below the angle of Louis (Morrison and Samwick) presented undoubted evidence of leukemic myeloblastosis. In addition, the constantly rising white blood cell count, which before death reached 300,000, left no doubt as to the nature of the condition.

Because of the peculiar resemblance of these early cells to cells of monocytic nature, it was difficult at the beginning to identify them as stem cells. With the demonstration of a positive oxidase reaction, their myeloblastic nature was established. Were it not for this fact, the cells could have been justifiably designated as monoblasts, and monocytic

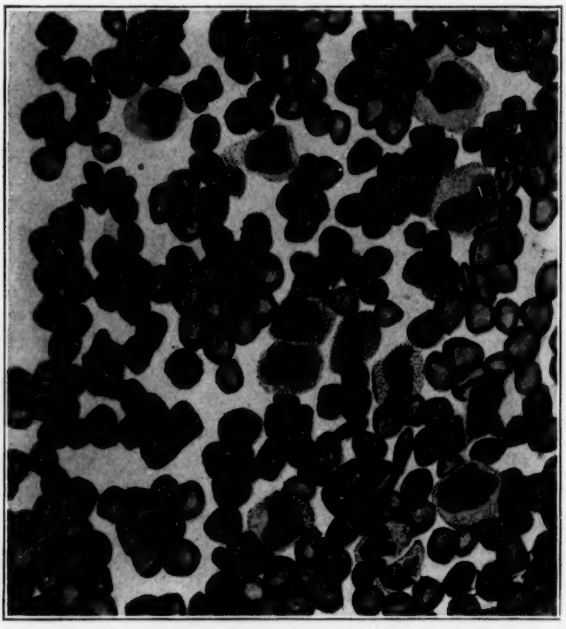

Fig. 2.—Microscopic drawing of peripheral blood smear.

leukemia could have been considered. The establishment, however, of the myeloid origin of the cells, made the term "monocytoid myeloblast" more descriptive, and the consideration of monocytic leukemia was dismissed. Furthermore, postmortem study showed a positive oxidase reaction for all the cellular infiltrations in the tissues of the various organs. In the course of the disease the cells became more easily recognizable as myeloid. At this point the diagnosis of congenital myeloblastosis was postulated with proper justification.

Aside from the cytologic characteristics in this case one was impressed with the two tumor masses, definitely not lymph nodes, which consisted of the clumps of densely packed infiltrations of cells previously

described. One of these masses had a typical green appearance on section. Such masses are considered as "chloromas" by many pathologists. But as this was clearly an instance of leukemia one is led to the more probable conclusion that such lesions are part and parcel of leukemia. The problem of whether "chloromas" should be regarded as leukemic tumor masses or as a symptom of generalized leukemia which is not recognizable at the time has not yet been solved. If the latter is true, then no patient with chloroma should be dismissed without a definite search for leukemic manifestations in the blood and bone marrow. In this case the tumor masses were discovered in the abdomen at autopsy. However, the large nodules on the skin of the back and scalp may be considered either as multiple chloromas or as leukemic nodules.

SUMMARY

A case of congenital leukemic myeloblastosis with "chloroma" has been described.

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CONGENITAL ABSENCE OF THE ABDOMINAL MUSCULATURE

ASSOCIATED CHANGES IN THE GENITOURINARY TRACT AND IN THE SPINAL CORD

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From an anatomic standpoint congenital absence of individual muscles is not rare. Shackleton [1] found absence of the palmaris longus muscle in 11.5 per cent of cases studied and of the pyramidalis muscle in 39.5 per cent. From a clinicopathologic point of view, however, only those muscular defects which produce functional disturbances or changes in the contour of the body are recognized. The most common site of such inborn muscular aplasia is the shoulder girdle, special predilection being evinced for the pectoral muscles. Of much less frequent occurrence is congenital absence of the abdominal muscles. This condition is of unusual interest because of commonly coexistent disorders in the genitourinary system.

The case reported is one of congenital absence of the abdominal musculature associated with hypertrophy of the urinary bladder, dilatation of both ureters and renal pelves and cryptorchidism.

REPORT OF A CASE

History.—F. S., a white boy aged 3 years, was admitted to the pediatric division of the Cook County Hospital on Jan. 14, 1937. The mother stated that the child had had a cough and fever for the past week, that during the past four days the abdomen, which had always been large, had become unusually distended and that the child had difficulty with urination.

The child was born at term, the birth weight being 6½ pounds (2,948 Gm.). Soon after birth it was noticed that the abdomen was unusually protuberant, that the abdominal musculature was absent and that the testicles were neither in the scrotum nor in the inguinal canal. When the child was 6 months of age the mother noticed blood in his urine on one occasion. He wore a binder to help

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1. Shackleton, W.: Report on the Presence of the Palmaris Longus, Plantaris, and Pyramidalis Abdominis, Tr. Roy. Acad. Med., Ireland **12**:401, 1894; cited by Bing, R.: Ueber angeborene Muskeldefecte, Virchows Arch. f. path. Anat. **170**:175, 1902.

support the abdominal wall. The dietary and developmental histories revealed nothing of significance.

Physical Examination.—The patient was well nourished and well developed. He appeared acutely ill. The temperature was 103.2, the pulse rate 136 and the respiratory rate 42. Examination of the head and neck gave negative results. The chest had the "pigeon breast" shape. Examination of the heart and the lungs revealed no abnormal findings. The abdomen was protuberant and distended, and it bulged in the flanks. The abdominal wall was thin, and on percussion an area of dulness was detected extending from the symphysis pubis to above the umbilicus. The extremities were normal, but the testes were undescended.

The initial diagnosis was congenital absence of the abdominal musculature associated with distention of the urinary bladder and nondescent of the testicles. The muscular defect was considered agenetic, and the possibility of a posterior urethral valve was considered as the cause of obstruction of the urinary tract. Catheterization yielded 1,400 cc. of dark urine. After catheterization the thinness of the abdominal wall was even more evident, as the abdominal viscera could be palpated easily.

The urinary retention continued to require daily catheterization, and as control was not obtained an indwelling catheter was inserted into the urinary bladder.

Cystoscopic study was performed on January 26 with the child under nitrogen monoxide anesthesia. The urinary bladder was found to be distended and atonic, and the mucosa was slightly inflamed. No urethral obstruction was seen. It was the impression of the consultant urologist that the urinary retention was caused by loss of the motor power and was neurologic.

Neurologic examination on January 27 showed the child to be fairly cooperative. He moved the head and the upper extremities fairly well and the lower extremities poorly. The pupils reacted to light and in accommodation, and the cranial nerves were normal throughout. The abdominal wall was soft and flabby, and when the head was raised the umbilicus moved upward (positive Beevor sign). The upper abdominal reflexes were present, but the lower ones were absent. The deep tendon reflexes in both the upper and the lower extremities were present, and pathologic signs were not elicited. The child resisted painful stimulation over all parts of the body. Over the sacral region a cutaneous sinus was seen. It was the neurologic consultant's impression that the disturbances were referable to dysraphia, that is, a type of developmental anomaly of the spinal cord, the pathologic lesion being in the nature of gliosis, a tumor or a cavity.

Laboratory Examination.—The hemoglobin content of the blood was 55 per cent. The red cell count was 3,950,000 and the white cell count, 17,150 per cubic millimeter. The differential count was normal. The Kahn test of the blood gave a negative reaction. The value for urea was 30.8 mg. per hundred cubic centimeters. The Wassermann reaction of the spinal fluid was negative. Roentgen examination of the lumbosacral portion of the spine showed no evidence of spina bifida. Intravenous pyelographic study on January 19 revealed dilatation of the right renal pelvis and calices, with dilatation and tortuosity of the ureter. Gas in the colon obscured the left renal pelvis.

Course.—While in the ward the child had pharyngitis, cervical lymphadenitis and an erythematous eruption. Cultures of material from the throat yielded Streptococcus haemolyticus. There was a septic temperature as high as 103 F. daily. He became listless and died on March 14.

Necropsy (Dr. R. H. Jaffé).—The anatomic diagnosis was congenital absence of the abdominal musculature; confluent bronchopneumonia of the right lower

pulmonary lobe; recent fibrinous peritonitis; bilateral hydroureter and hydronephrosis; hypertrophy of the wall of the urinary bladder; cecum mobile, and bilateral cryptorchidism.

Macroscopic Observations: The abdomen was protuberant, and the scrotum was small and empty. The fat at the midline measured 8 mm. in thickness. When the abdominal cavity was opened the intestinal loops were seen to be matted together by loose, light yellow-gray membranes. The cecum and the vermiform appendix were observed near the midline below the left lobe of the liver. The cecum, the appendix, the ascending colon and the ileum had a common mesentery

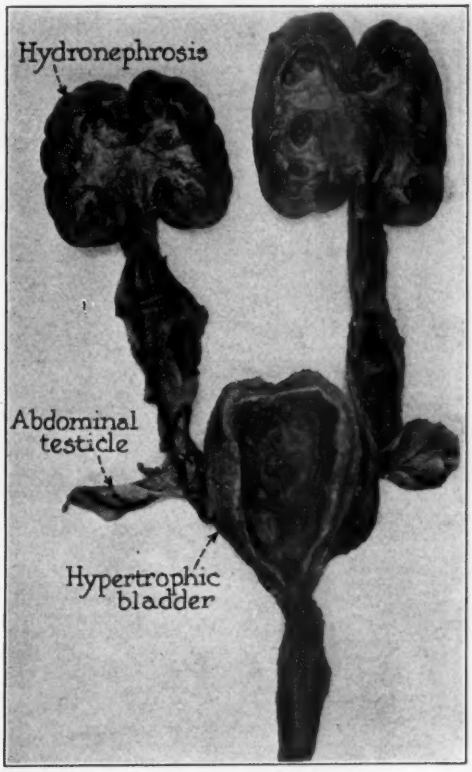

Fig. 1.—Photograph of the genitourinary system, showing dilatation of the urinary passages and abdominal localization of the testicles.

which permitted free motility of these structures. The urinary bladder was distended up to 7.5 cm. above the symphysis pubis. The kidneys weighed 210 Gm., and the renal pelves were dilated, especially the left. Both ureters were long, tortuous and dilated, the left ureter measuring up to 40 mm. in circumference, the right up to 26 mm. (fig. 1).

The urinary bladder was distended, the wall averaging 8 mm. in thickness. The ureteral openings were in their normal positions and were patent. The urethra was patent throughout. The testicles were present at the brim of the pelvis. They measured 15 by 10 by 6 mm. and 20 by 6 by 6 mm. in diameter, respectively.

The anterior layer of the parietal peritoneum seemed to rest directly on the subcutaneous fat tissue, being separated from it by a layer of fascia.

Microscopic Observations: Sections taken from different areas of the anterior abdominal wall (fig. 2) disclosed the following layers: There was a well differentiated epidermis with short rete pegs resting on a thick cutis which contained many sweat glands. Beneath the cutis was a thick layer of fat tissue which was traversed by branching septums of dense connective tissue. In the deeper layers of the fat tissue these septums were fused, merging into a fairly thick and dense fascia, which stained deep purple-red with the Van Gieson stain. Beneath this

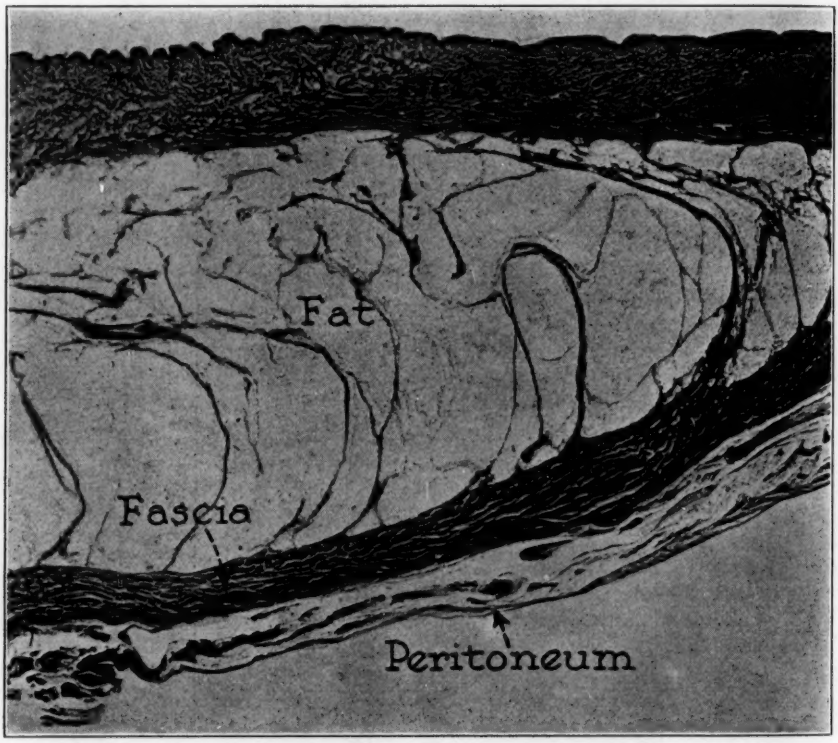

Fig. 2.—Low power photomicrograph of the anterior abdominal wall, showing the complete absence of muscle tissue. (Van Gieson's stain.)

fascial plane were numerous thick-walled blood vessels followed by a second layer of fascia, which overlay the peritoneum. No evidence of striated muscle was found. With Weigert's elastica stain both layers of fascia as well as the branching connective tissue trabeculae of the subcutaneous fat tissue were seen to contain elastic fibers.

In sections of spinal cord stained by the Kultschitzky-Pal method the white matter was seen to be unchanged, and the gray matter at the various levels was of normal configuration. The only changes which could be considered pathologic were seen in the anterior horns of the lower thoracic levels in sections stained with toluidine blue. In these regions the motor ganglion cells were slightly

decreased in number, and some of them were diminished in size (fig. 3). Many of the small ganglion cells were elongated and tadpole shaped, their cytoplasm being filled with closely packed granules of chromatin material. The nuclei in these cells were small and pyknotic. The diminution in the size of the cells was not limited to any cell group but varied greatly in the different levels and in different parts of the same level. The ganglion cells in the lateral and posterior columns as well as in Clarke's columns showed no significant changes. The gliocytes were everywhere normal in appearance, showing neither proliferative nor degenerative changes.

Fig. 3.—Low power photomicrograph of a lower thoracic segment of the spinal cord. Many of the ganglion cells in the anterior horn (*A.H.*) are small and atrophic. *C.C.* indicates the central canal. (Toluidine blue stain.)

The leptomeninges were thin and free from cellular infiltrations, and the dura mater as well as the various spinal roots was unchanged.

COMMENT

One distinguishes two groups of conditions productive of dilatation of the upper urinary passages and hypertrophy of the urinary bladder, namely, obstruction and neurogenic dysfunction. Whereas in the former

there is an apparent obstruction to the escape of the vesical contents or the history of the presence of such an obstruction which had been relieved spontaneously or operatively sometime before, the latter is characterized by absence of obstructive factors and the presence of some disorder of the nervous system. Despite the comprehensive literature on this subject, there still remains a group of cases in which hypertrophy of the urinary bladder with or without dilatation of the upper urinary passages occurs when there is neither an obstruction nor evidence of neurogenic dysfunction either clinically or pathologically. To this group belong those cases in which the changes in the urinary tract are associated with congenital defects of the abdominal musculature. Writing of such cases, Stumme [2] in 1903 stated that late in embryonic life occlusion of the urethra occurs, causing retention of urine, and that the bladder and ureters respond by dilation and hypertrophy. He concluded that the much dilated urinary bladder then causes pressure atrophy of the abdominal musculature. He stated that the cause of the urinary retention later disappears. Garrod and Davies [3] in 1905 concluded, similarly, that the condition of the abdominal musculature is secondary to dilatation of the urinary bladder.

There are two objections to these views: First, the exact nature of the urinary obstruction is not stated, and, secondly, in the reported cases of marked distention of the urinary bladder of the fetus in utero due to congenital atresia or valvular obstruction of the urethra (Schmidt [4]) no mention is made of absence of the abdominal musculature. Guthrie,[5] who in 1896 reported a case of congenital absence of the abdominal musculature, found fixation of the urinary bladder to the anterior abdominal wall in addition to the muscular deficiency. He stated the belief that the urinary bladder became hypertrophic because its fixation to the abdominal wall prevented it from contracting and emptying itself. Such an explanation, however, is inapplicable to the case reported here, because the urinary bladder was not fixed to the anterior abdominal wall.

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2. Stumme, E. G.: Ueber die symmetrischen kongenitalen Bauchmuskeldefekte und über die Kombination derselben mit anderen Bildungsanomalien des Rumpfes, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **11**:548, 1903.

3. Garrod, A. E., and Davies, L. W.: On a Group of Associated Congenital Malformation, Including Almost Complete Absence of the Muscles of the Abdominal Wall, and Abnormalities of the Genito-Urinary Apparatus, Med.-Chir. Tr., London **88**:363, 1905.

4. Schmidt, C. O.: Ein Fall von hochgradiger Dilatation der Harnblase, der Harnleiter und Nierenbecken infolge eines klappenartigen Verschlusses des Orificium urethrae internum, Ztschr. f. urol. Chir. **11**:158, 1923.

5. Guthrie, L.: Case of Congenital Deficiency of Abdominal Muscles, Tr. Path. Soc., London **47**:139, 1896.

Bardeen [6] in the discussion of a similar case reported by Osler [7] in 1901 stated that the lack of resistance normally met with in the abdominal wall by the urinary bladder may cause it to expand rather than to contract and empty its secretions into the amniotic fluid.

Many theories have been proposed to explain the muscular deficiency. Scammon,[8] expressed the belief that it is due to failure or arrest of forward extension of the embryonal skeletal muscle tissue into the anterior abdominal wall. Bardeen [6] stated that whereas under normal conditions the growth of the abdominal musculature is preceded by the formation of a vascular plexus, an abnormal arrangement of the plexus might impede its growth. Others have interpreted the abdominal muscular defects in the same light as the defects in other muscle groups, namely, as aplastic or dysplastic malformations. Even localized intrauterine muscular dystrophy and a neurogenic cause for the muscular deficiency have been suggested.

From the histologic study of the abdominal wall in this case the complete absence of the abdominal musculature without traces of either a connective tissue scar or atrophic or dystrophic muscle fibers speak rather for congenital absence than for pressure atrophy or fetal muscular dystrophy.

The changes in the spinal cord were minimal in extent, so that it is difficult to evaluate their significance. As the motor ganglion cells which innervate the various groups of abdominal muscles are scattered through various levels of the spinal cord in close relation to the ganglion cells innervating the musculature of the back and as the ganglionic cellular alterations are not restricted uniformly to one cell column, I do not believe that the changes described are of great significance. Diminution in the size and number of the motor ganglion cells has been described as following amputations (Marinesco [9]) and as associated with congenital absence of an extremity (Elders [10]). Such changes seem to indicate that the continued life of the neuron is dependent on the per-

6. Bardeen, cited by Osler.[7]

7. Osler, W.: Congenital Absence of the Abdominal Muscles with Distended and Hypertrophied Urinary Bladder, Bull. Johns Hopkins Hosp. **12**:331, 1901.

8. Scammon, R. E., cited by Ikeda, K., and Stoesser, A. V.: Congenital Defect in the Musculature of the Abdominal Wall, Am. J. Dis. Child. **33**:286 (Feb.) 1927.

9. Marinesco, G.: Ueber die durch Amputation hervorgerufenen Veränderungen der Nerven und des Rückenmarks, Berl. klin. Wchnschr. **29**:988, 1892.

10. Elders, C.: Die motorischen Centren und die Form des Vorderhorns in den fünf letzten Segmenten des Cervikalmarks und dem ersten Dorsalsegmente eines Mannes, der ohne linken Vorderarm geboren ist, Monatschr. f. Psychiat. **28**:491, 1910.

formance of the normal functions of all its parts. Whereas Schlesinger [11] found similar changes in a case of congenital muscular deficiency (pectoral group), Obersteiner [12] found minimal changes which he believed to be well within the range of normal variability in the size and number of the motor ganglion cells. As the ganglionic changes following amputation, for example, develop over a period of years, it may be that the age of the person or other factors determine the degree and extent of ganglionic cellular change in cases of congenital muscular deficiency. I cannot help but interpret the few changes present in my case as evidences of such so-called retrograde degeneration. The changes are not really degenerative but correspond more nearly to atrophy from disuse.

Such conditions must, of course, be differentiated from primary aplasia of motor ganglion cells, a condition described years ago by Mobius.[13] The constant presence of the external ocular musculature in the cases of anencephaly that came under my observation and Leonowa's [14] observation of the presence of normal striated skeletal and ocular musculature in a case of anencephaly and amyelia indicate that the presence of motor ganglion cells is not necessary for the initial development of the skeletal musculature.

As the changes in the spinal cord do not indicate a neurogenic cause for the vesical changes and the changes in the upper portion of the urinary tract, I believe these changes to have been obstructive. As the anomaly of the urinary tract is already present at birth in such cases, the obstruction must be already present in utero.

Under normal conditions micturition is accomplished by the combined effects of the contraction of the detrussor muscle of the urinary bladder and the rise in intra-abdominal pressure produced by the contraction of the abdominal muscles and the diaphragm. In a case of congenital absence of the abdominal muscles, studied by Mackeith and his co-workers,[15] roentgen examination of the genitourinary tract revealed nothing abnormal, but the patient, a boy, could not completely empty his urinary bladder. More marked urinary disturbances were present

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11. Schlesinger, H.: Zur Lehre von angeborenem Pectoralis-Reppendefect und dem Hochstande der Scapula, Wien. klin. Wchnschr. **13**:25, 1900.

12. Obersteiner, H.: Rückenmarksbefund bei Muskeldefekten, Wien. klin. Rundschau **16**:302, 1902.

13. Mobius, P. I.: Ueber infantilen Kernschwund, München. med. Wchnschr. **39**:17, 1892.

14. von Leonowa, O.: Zur pathologischen Entwicklung der Centralnervensystems: Ein Fall von Anencephalie combiniert mit total Amyelia, Neurol. Centralbl. **12**:218 and 263, 1893.

15. Mackeith, N. W.; Spurrell, W. R.; Warner, E. C., and Westlake, H. J. W. J.: Observations on a Boy with Congenital Deficiency of the Anterior Abdominal Wall Muscles, Guy's Hosp. Rep. **73**:479, 1923.

in the case described in this paper, in which the urinary bladder became so distended that catheterization was necessary. In these cases the accessory forces used in micturition were absent, as the relaxation of the anterior abdominal wall precluded a rise in the intra-abdominal pressure even with a marked contraction of the diaphragm. It is my belief that the fetus in utero utilizes similar accessory forces in the process of micturition. Ahlfeld,[16] who studied the respiration of the fetus in utero, succeeded in getting graphic tracings with the cardiograph showing that when the chest expands the abdomen contracts. With absence of the abdominal musculature such accessory forces would be lacking. Whereas the child with such a condition normally has difficulty emptying its urinary bladder, for the fetus in utero the difficulty is even greater, as the intrauterine pressure, that is, the pressure in the amniotic fluid, is definitely greater than the atmospheric pressure.

The sequence of events in the development of changes in the urinary tract is, I believe, as follows: The urine excreted by the fetal kidneys is stored in the urinary bladder. The lack of the accessory forces of micturition and the increase in the external (amniotic) pressure prevent emptying of the urinary bladder. Distention of the bladder occurs, followed by hydroureter and hydronephrosis. In time the fetal urinary bladder becomes hypertrophic, and then it is able to empty its contents into the amniotic fluid. The evidence of its former incompetence remains permanently in the form of hydroureter and hydronephrosis. In some cases, for example in that recorded by Ikeda and Stoesser,[17] hypertrophy of the urinary bladder was the only change in the urinary system. The ureters were not dilated. Such a condition indicates, I believe, that the urinary bladder became hypertrophic before sufficient back pressure developed to produce hydroureter and hydronephrosis.

The conditions which would determine the degree of change in the urinary tract would depend on several variable factors difficult to evaluate, such as the intrauterine pressure, the amount of urine secreted by the fetal kidneys and the ability of the fetal bladder to become hypertrophied and expel its contents. Though the dilated and tortuous ureters with their mucosal folds resembling the valvulae conniventes of the small intestine may suggest a giant growth of the urinary tract, identical states have been seen in cases of long-standing urinary obstruction in children due to valves in the urethra (Counseller and Menville [18]).

16. Ahlfeld, cited by DeLee, J. B.: The Principles and Practice of Obstetrics, ed. 6, Philadelphia, W. B. Saunders Company, 1933, p. 59.

17. Ikeda, K., and Stoesser, A. V.: Congenital Defect in the Musculature of the Abdominal Wall, Am. J. Dis. Child. **33**:286 (Feb.) 1927.

18. Counseller, V. S., and Menville, J. G.: Congenital Valves of the Posterior Urethra, J. Urol. **34**:268, 1935.

With the exception of a single case, reported by Hofstein,[19] all of the instances of congenital absence of the abdominal musculature have occurred in males. In addition to anomalies of the urinary tract, these cases have been characterized by nondescent of the testicles. It may be that the relaxation of the anterior abdominal wall in preventing an adequate rise in the intra-abdominal pressure produces a lack of the normal vis a tergo necessary for their proper descent.

SUMMARY

A case of congenital absence of the abdominal musculature, associated with hypertrophy of the urinary bladder, dilatation of the ureters and the renal pelves and bilateral cryptorchidism is presented.

The muscular defect is interpreted as aplastic.

Diminution in the size and number of the motor ganglion cells in the anterior horns of the lower thoracic levels of the spinal cord is attributed to so-called retrograde degeneration of the ganglion cells or atrophy from disuse.

The changes in the urinary tract are interpreted as obstructive, though cystoscopically they suggested neurogenic dysfunction, and a theory as to the development of this anomaly is presented.

The bilateral cryptorchidism was probably due to diminution in the normal vis a tergo necessary for the proper descent of the testicles.

19. Hofstein, J.: Absence congénitale des muscles abdominaux chez un nouveau né du sexe feminine, Gynéc. et obst. **22**:23, 1930.

ACUTE HEMOLYTIC ANEMIA

LEDERER TYPE

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The literature has several excellent reports of Lederer's anemia.[1] We recently observed a case which is identical in type with those originally described by Lederer.

REPORT OF A CASE

J. G., a boy of Jewish extraction, 25 months of age, was admitted to the Jewish Memorial Hospital on May 6, 1938. He had been in excellent health until February 1938, at which time bilateral myringotomy was performed for otitis media. His recovery from this illness was rapid and uneventful. His parents were in excellent health and had no history of chronic illness. On May 1 the infant suddenly became acutely ill, with elevation of temperature to 103 F. and continuous vomiting. Three days later the mother observed a yellowish tinge of the boy's skin and became alarmed because of his extreme pallor and listlessness. One of us (W. L.) saw the patient with the family physician, Dr. L. Rosenblum, on the day of admission to the hospital. The child was well nourished; he was semicomatose and had marked pallor of the skin and mucous membranes. The temperature was 101.8 F. and the pulse rate 170 per minute. Slight icterus of the skin and of the bulbar conjunctivas was noted. The ears were normal except for paracentesis scars. No ulcerations were present in the mouth. The spleen was palpable 1 fingerbreadth below the costal margin. All other physical findings were unimportant. Hematologic study at 4 p. m. revealed severe secondary anemia. The hemoglobin content was 21 per cent (Sahli); red cells numbered 1,380,000 per cubic millimeter and white cells 16,900. The differential count revealed 50 per cent segmented polymorphonuclears, 10 per cent nonsegmented polymorphonuclears, 25 per cent lymphocytes, 10 per cent monocytes, 4 per cent myelocytes, 1 per cent basophilic myelocytes, 4 per cent normoblasts and 4.9 per cent reticulocytes. Smears showed poikilocytosis and anisocytosis. There was no history of ingestion of drugs or other poisonous materials to explain this severe hemolytic crisis. Immediate hospitalization was advised.

Six hours later, on the patient's admission, a second blood count was done; the hemogram was essentially identical with the first except for elevation of the

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From the Pediatric Service of Dr. Michael Schuman, Jewish Memorial Hospital.

1. (*a*) Lederer, M.: A Form of Acute Hemolytic Anemia Probably of Infectious Origin, Am. J. M. Sc. **170**:500, 1925; (*b*) Three Additional Cases of Acute Hemolytic (Infectious) Anemia, ibid. **179**:228, 1930. (*c*) Josephs, H. W.: Anemia of Infancy and Childhood, Medicine **15**:3, 1936.

Results of Examination of the Blood of a Child with Acute Hemolytic Anemia

Date	Hemoglobin	Red Cells, Million per Cu. Mm.	White Cells, Thousand per Cu. Mm.	Segmented Polymorphonuclears, %	Nonsegmented Polymorphonuclears, %	Eosinophils, %	Basophils, %	Lymphocytes, %	Monocytes, %	Myeloblasts, %	Myelocytes, %	Metamyelocytes, %	Normoblasts, %	Reticulocytes, %	Poikilocytosis	Anisocytosis	Hypochromia	Polychromia	Myelocytic Basophilia, %	Plasma Cells	Türk's Cells	Platelets, No. per Cu. Mm.	Peroxidase Cells, %	Hematocrit Reading	Volume Index	Icteric Index	Van den Bergh Reaction, Direct and Indirect
5/6 4 p. m.	21% 3.4 Gm.	1.38	16.9	50	10	..	..	25	10	..	4	..	4	4.9	+	+	..	..	1	..	..	..	..	..	..	..	..
5/6 10 p. m.	24% 3.9 Gm.	1.35	63.1	58	9	..	1	25	2	..	3	2	1	..	+	+	..	..	..	..	..	..	..	..	..	..	..
5/7	37% 6 Gm.	2.11	47.0	54	5	..	1	32	5	..	1	2	11	1	+	+	+	+	..	..	..	310,000	..	..	..	..	..
5/9	53% 85 Gm.	2.89	18.4	56	10	3	..	19	6	2	2	2	1	1.9	+	Marked	..	..	..	..	..	..	..	..	..	..	..
5/10	57% 9 Gm.	2.86	8.45	48	5	5	..	36	4	..	2	..	..	1.4	+	+	..	Marked	..	..	..	..	..	..	..	..	..
5/11	60% 9.5 Gm.	3.21	13.25	49	12	1	1	32	2	1	1	1	..	1.8	+	+	..	Marked	..	..	..	..	..	..	..	..	..
5/12	53% 8.5 Gm.	3.61	7.65	54	5	2	..	30	6	1	..	..	..	..	..	..	..	..	..	2	..	240,000	..	..	..	5.0	Normal
5/13	71% 11.5 Gm.	3.85	12.3	68	4	1	1	22	4	..	..	..	1	..	..	..	..	Slight	..	..	..	320,000	..	..	..	..	..
5/14	68% 11 Gm.	3.68	12.7	62	2	1	..	28	6	..	..	..	..	..	..	..	..	Slight	..	..	1	..	..	..	..	..	..
5/16	57% 9 Gm.	3.32	6.3	39	2	1	..	56	2	..	..	..	..	..	+	+	+	..	..	..	..	..	..	..	..	7.0	Normal
5/17	53% 8.5 Gm.	3.24	6.55	50	1	..	..	49	..	..	..	..	..	..	..	..	..	..	..	..	..	..	50	..	..	..	..
5/18	57% 9 Gm.	3.47	.....	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	3.4	1.18 80% Normal	3.5	Normal
5/20	65% 10.5 Gm.	3.65	8.95	44	3	..	1	50	2	..	..	..	..	..	+	+	+	..	..	..	..	..	..	..	..	..	..
5/21	.....	....	.....	..	..	..	..	..	..	..	..	..	..	1.4	..	..	..	..	..	..	..	..	..	..	..	..	..
5/23	62% 10 Gm.	3.92	6.8	35	5	2	..	56	2	..	..	..	..	..	..	..	+	..	..	..	..	..	..	..	..	..	..
5/24	63% 10.3 Gm.	3.84	8.1	38	1	..	..	58	3	..	..	..	..	..	..	..	+	..	..	..	..	..	..	..	..	..	..
6/1	65% 10 Gm.	3.62	6.2	55	5	1	..	38	1	..	..	..	..	..	Slight	Slight	Slight	..	..	..	.	..	..	..	..	..	..
6/10	75% 12 Gm.	3.81	5.6	33	1	3	..	58	5	..	..	..	..	..	..	..	Slight	..	..	..	..	..	..	..	..	..	..
6/22	71% 11.5 Gm.	4.4	7.55	41	1	2	..	60	4	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..

white cell count to 63,100. This study was followed by transfusion, 200 cc. of citrated blood being given. A continuous intravenous infusion of 5 per cent dextrose in saline solution was administered after the transfusion. The response to this therapy was spectacular. In contrast to the clinical picture presented on his admission, within twelve hours the child was alert, the icteric tint had disappeared, and the pallor was no longer extreme. Thirty-six hours after admission the temperature was normal, and the spleen could no longer be palpated. A second transfusion was performed, 200 cc. of citrated blood being given, on the day after admission.

Graphic evidence of the rapid response to transfusion is presented by the laboratory data in the accompanying table. The fragility test showed that hemolysis began with a 0.45 per cent saline solution and was incomplete with a 0.3 per cent solution. No sickling of the red cells was noted. The hematocrit reading was 3.4 and the volume index 1.18, or 80 per cent of the normal value. The icteric index varied between 3.5 and 7.0. The reactions to the direct and the indirect van den Bergh test were normal on several occasions. Sternal puncture was performed. The bone marrow revealed normal constituents and did not disclose any evidence of blood dyscrasia. Results of Wassermann, Mantoux and Schick tests and of examinations of the stool were all negative. The urine was normal. Examination on May 7, one day after the patient's admission, showed that urobilinogen was present in a 1:10 dilution. None was present in the urine on subsequent testing. Roentgen study revealed that the long bones were normal. The parents submitted to complete study of their blood, which did not reveal any abnormalities.

During the remainder of his stay in the hospital the child received large amounts of iron and ammonium citrates and liver. He made an uneventful recovery and was discharged from the hospital on May 25. He has enjoyed excellent health since that time.

Subsequent hemograms are charted in the table.

COMMENT

This hemolytic crisis, according to Josephs,[1c] may be caused by mild or severe infection, paroxysmal hemoglobinuria, favism, blackwater fever associated with malaria, transfusion of mismatched blood, vaccination, gas poisoning or ingestion of drugs or allergic materials. Harvey and Janeway [2] recently reported a case of acute hemolytic anemia which followed the ingestion of sulfanilamide; they commented on the similarity of their case to those described by Lederer. Greenthal [3] recovered Streptococcus haemolyticus from the blood stream of a patient who responded to sulfanilamide therapy and transfusions. The blood picture of congenital hemolytic jaundice or of pernicious anemia may be confused with that of acute hemolytic anemia. Pernicious

2. Harvey, A. M., and Janeway, C. A.: The Development of Acute Hemolytic Anemia During the Administration of Sulfanilamide (Para-Aminobenzenesulfonamide), J. A. M. A. **109**:12 (July 3) 1937.

3. Greenthal, R. M.: Acute Hemolytic Anemia Developing During Streptococcus Sepsis, J. Pediat. **12**:517, 1938.

anemia is rarely seen in children.[1c] The fragility test has been offered as a diagnostic aid in distinguishing between the blood crisis of congenital hemolytic jaundice and that of acute hemolytic anemia. However, Josephs [1c] has been inclined to dispute the specificity of this procedure.[4] The spectacular and permanent response to transfusion is characteristic of acute hemolytic anemia.

Our case clinically and hematologically resembles the reported cases of Lederer, in that the child had an acute onset with marked erythrocytic destruction, rapid stimulation of the bone marrow and prompt response to transfusion. As in his cases, our patient did not experience sequelae or relapses. We also believe that in the absence of any demonstrable etiologic agent, infection apparently offers the most logical explanation. The presence of fever, leukocytosis, a palpable spleen and anemia are presumptive evidence in support of this conclusion. Parsons and Hawksley [5] expressed the opinion that infection is the responsible factor in the production of this syndrome, even though they were unable to detect any specific cause. Poisonous drugs, allergic substances or other disease entities were not responsible for the symptoms in the present instance.

Josephs cited a case in which the red blood cell count was 600,000. Our lowest reading was 1,350,000. In the presence of such a severe anemia, with a hemoglobin content as low as 21 per cent, the color index was high. This is characteristic. Lazarus,[6] Lederer [7] and Kaiser and Bradford [8] reported cases in which there was hyperleukocytosis, the count varying between 52,000 and 108,000. We found 63,100 leukocytes per cubic millimeter before transfusion. After the administration of blood there was a rapid decrease in the number of leukocytes. The lymphocytes were all mature. Various forms of immature cells of the myeloid and erythrocytic groups were found in the peripheral blood in the first few days of illness. These had all disappeared one week after transfusion. Changes in the size, shape and hemoglobin content of the red blood cells were noted, as indicated in the table. Platelets are not

4. Holst, P. T.: Acute Hemolytic Anemia, Acta med. Scandinav. (supp.) **26**:469, 1928. Nixon, N. K., and Vaughn, J. O.: Hemoglobinuria in Childhood Following Acute Tonsillar Infection, Am J. Dis. Child. **49**:710 (March) 1935.

5. Parsons, L. G., and Hawksley, J.: The Hemolytic (Erythronoclastic) Anemias with Special Reference to the Acute Hemolytic Anemia of Lederer and the Anemia of Von Jaksch, Arch. Dis. Childhood **8**:184, 1933. Parsons, L. G.: The Anemias of Infancy and Early Childhood: Some Observations, J. A. M. A. **97**: 973 (Oct. 3) 1931.

6. Lazarus, S. D.: Acute Hemolytic Anemia in Childhood, Am. J. Dis. Child. **40**:1063 (Nov.) 1930.

7. Footnote 1 *a* and *b*.

8. Kaiser, A. D., and Bradford, W. L.: Acute Hemolytic Anemia, Arch. Pediat. **46**:571, 1929.

affected ordinarily but may be reduced.[1c] The thrombocytes in our studies were normal. The reticulocyte count was high on the patient's admission and with recovery became normal.

SUMMARY

A case of hemolytic anemia of the Lederer type is reported.

No cause was found. Infection presumably offers the best explanation for this symptom complex.

Spectacular response to transfusion was noted.

ANOMALOUS DRAINAGE OF PULMONARY VEINS INTO CORONARY SINUS

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Anomalies of the pulmonary veins, particularly of the isolated type, constitute one of the rare groups of congenital cardiac defects. Such examples as have been reported can be classified into (1) anomalies in number, (2) anomalies in drainage and (3) anomalies in number and drainage. Of most practical interest are those anomalies of the pulmonary veins which involve a variation in drainage. Instead of terminating in the left atrium, one or more of the pulmonary veins may empty into remnants of the fetal circulation (left superior vena cava, ductus venosus), the systemic veins (superior vena cava, inferior vena cava, azygous, innominate and subclavian veins), the portal system, the right atrium or the coronary sinus.

At present, the available literature yields only 3 cases [1] of anomalous drainage of all the pulmonary veins into the coronary sinus as a primary developmental lesion. Because of this rarity I wish to record the pathologic observations on an additional specimen of the anomaly, which was noted in a 5½ month old boy.

REPORT OF A CASE

History.—R. D., an American boy aged 5½ months, was admitted to the Children's Hospital on April 3, 1937, because of frequent emesis and edema of the legs.

The father and mother, 31 and 27 years of age, respectively, were in good health. The patient was the second of two children. A sister, 3 years old, was alive and well. The mother had had one miscarriage. The patient was born at full term and weighed 7 pounds (3,175 Gm.). There was no evidence of cyanosis at birth. After each breast feeding, the infant vomited. When bottle feeding was begun, six weeks before entry to the hospital, he ceased to have emesis but did not gain weight. The feet had been swollen for three weeks. There was a history of attacks of "bronchitis."

From the Pathological Laboratory, Buffalo General Hospital, Children's Hospital and the University of Buffalo School of Medicine (Dr. K. L. Terplan, Director).

1. (*a*) Nbarro, D.: Two Hearts Showing Peculiarities of the Great Veins, J. Anat. **37**:382, 1903. (*b*) De Groat, A. F., and Thatcher, H. S.: Congenital Anomaly of Heart: Both Pulmonary Veins Emptying into Coronary Sinus, J. Tech. Methods **16**:93, 1936. (*c*) Nagel, A.: Eine Transposition aller Lungenvenen in den rechten Vorhof, Virchows Arch. f. path. Anat. **297**:343, 1936.

Physical Examination.—The temperature was 98 F., the pulse rate 145 and the respiratory rate 42. The length of the body was 24½ inches (62 cm.), the width 5½ inches (14 cm.) and the weight 11 pounds (4,990 Gm.). The infant appeared extremely anemic and was definitely dehydrated. The anterior fontanel was open. The tongue was coated and dry. The chest was clear and resonant. The heart was not found to be enlarged. No thrills or murmurs were detected. The liver reached 4 fingerbreadths below the costal margin. The spleen was not palpable. The ankles showed pitting edema.

Course.—About thirty-six hours after admission the infant died during a cyanotic attack.

Postmortem Examination.—This was performed by Dr. Terplan and myself two hours after death. The pathologic diagnosis was congenital heart disease with anomalous drainage of the pulmonary veins into the coronary sinus; marked passive hyperemia of the liver, spleen, kidneys and gastrointestinal tract; low position of the diaphragm; distinct thickening of the walls of the pulmonary arterioles, and duplex kidney on the left.

Description of Heart: On removal of the sternum, the pericardium was seen to be distinctly distended. Pericardial fluid was not increased in amount. The heart was markedly enlarged. This enlargement involved the right atrium, right auricular appendage and right ventricle. The left atrium and ventricle were small and were rotated posteriorly. The heart assumed a horizontal position and quadrilateral shape. The vertical, horizontal and anteroposterior diameters were each 6 cm.

The superior vena cava was 2 cm. in length and 1 cm. in circumference. The innominate, jugular and azygous veins opened in their regular sites. Just below the orifice of the azygous vein, the intima of the superior vena cava showed a slight dimple. The direction and entrance of the superior and inferior venae cavae into the right atrium were normal. The valve of the inferior vena cava was well developed. Its right margin was lost in the wall of the atrium; its left margin was continuous with a well developed limbus fossae ovalis. The fossa ovalis itself was markedly depressed. It measured 1 by 0.7 by 0.6 cm. That portion of the sinus venarum bounded by the superior and inferior venae cavae, eustachian valve and limbus fossae ovalis almost seemed to form a separate third division of the right atrium. In the fossa ovalis was a small foramen ovale, like a crescentic slit, measuring 0.3 by 0.2 cm.

Between the eustachian and the tricuspid valve, anterior and medial to the inferior vena cava, was the markedly enlarged orifice of the coronary sinus, which was 1.5 cm. in circumference. Partially overhanging the opening there was a thin, membranous thebesian valve, which took origin about 0.3 cm. from the juncture of the limbus fossae ovalis and the eustachian valve. The anterior margin of the orifice of the sinus was 0.3 cm. from the tricuspid valve. Dissection of the coronary sinus revealed it to be a large cavity measuring 2 by 2.5 cm. with a thick, opaque wall. Two short pulmonary veins opened into the sinus. Each of these, left and right, was formed by tributaries from respective lobes (two on the left and three on the right with two additional small vessels from the lower lobe). The coronary sinus also received the great cardiac vein, the middle cardiac vein (just before the entrance of the sinus into the right atrium), the oblique vein (0.9 cm. from the opening of the great cardiac vein) and two atrial veins. The cavity of the right atrium was 5.7 cm. in circumference; its wall was 0.2 cm. thick.

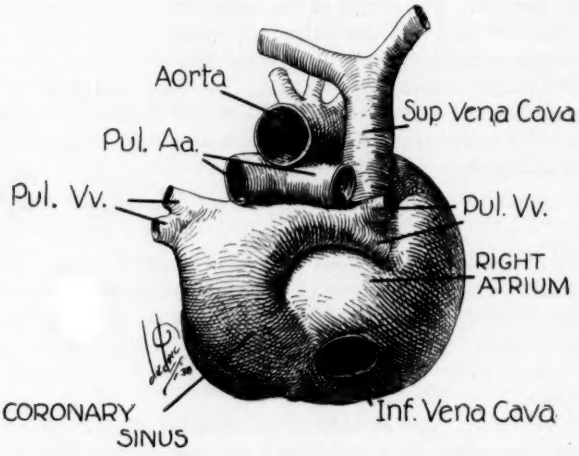

Fig. 1.—Diagram showing pulmonary veins draining into the markedly dilated coronary sinus. (One tributary of the right pulmonary vein is not shown in the plane of the diagram.)

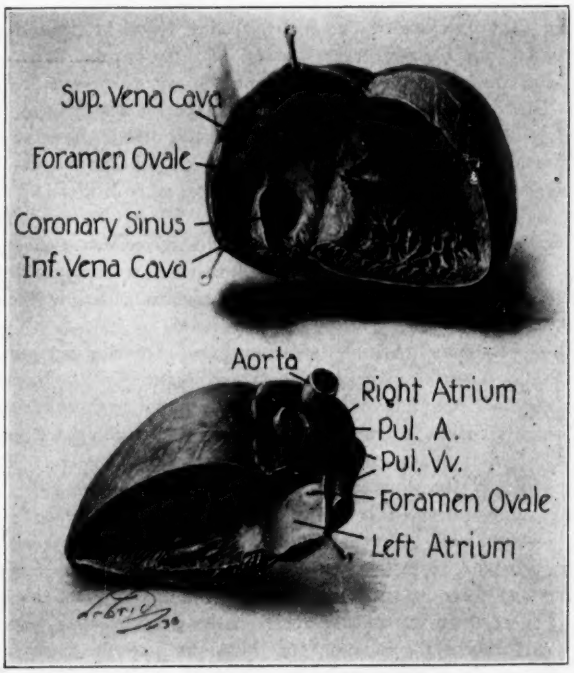

Fig. 2.—Interior views of the right and left sides of the heart in a case of anomalous drainage of the pulmonary veins into the coronary sinus.

The right auricular appendage was markedly dilated. It measured 6.2 by 0.3 cm. The wall was 0.15 cm. thick. The musculi pectinati were prominent. The tricuspid valve was 5.2 cm. in circumference. The leaflets and the chordae tendineae were thin and delicate. The wall of the right ventricle was hypertrophic, being 0.7 cm. thick. The cavity was dilated; it was 5.3 cm. in circumference. There was slight endocardial fibrosis. The conus arteriosus was rounded and hypertrophic. The trabeculae carneae were hypertrophic. The anterior papillary muscle measured 2.2 by 1.8 cm. The pulmonary artery was dilated, being 3.7 cm. in circumference. Its valve and branches were normal.

The left atrium was small. The wall was 0.1 cm. thick; the cavity measured 2.5 by 1.8 cm. No veins opened into the left atrium. The foramen ovale was protected by a well formed thick nonadherent valve. The left auricular appendage measured 1.5 by 1.5 cm. The mitral valve was 2.5 cm. in circumference. The cavity of the left ventricle was 3.5 cm. in circumference; the wall was 0.5 cm. thick. The trabeculae carneae were very thin. The papillary muscles measured 1.5 by 0.4 cm. The aortic cusps were normal. The coronary arteries had the usual origin and number. The aorta measured 2.1 cm. above the valve and 1.2 cm. at the isthmus. The ductus arteriosus could not be probed. It was grossly obliterated in its midpart; it possessed dimpled ends in the aorta and in the pulmonary artery.

COMMENT

In addition to disclosing the rarity of anomalous drainage of the pulmonary veins into the coronary sinus, review of the 3 reported cases with that presented here raises four provocative questions.

1. Even on the basis of only 4 cases, can anomalous drainage of the pulmonary veins into the coronary sinus be considered as representing a distinct entity in the scheme of congenital heart disease? Except for the number of pulmonary veins which entered the coronary sinus, the anatomic features in all recorded cases were practically identical. The coronary sinus was dilated and its wall thickened. The orifice of the sinus was enlarged. The right side of the heart, including the atrium, auricular appendage and ventricle, showed marked dilatation and hypertrophy. The left atrium and ventricle were small. The circumference of the pulmonary artery was widened. Special note must be made of the regular presence of the small foramen ovale and the grossly impervious ductus arteriosus. In Nbarro's case [1a] the pulmonary veins terminated in the coronary sinus as four separate vessels, in the case of De Groat and Thatcher [1b] as one trunk, and in the case of Nagel [1c] and in my case as two stems. Undoubtedly, then, anomalous drainage of the pulmonary veins into the coronary sinus must be recognized on anatomic grounds as a specific cardiac malformation.

2. Do the anatomic features, just shown to be of constant occurrence, produce corresponding clinical effects of such uniformity as to suggest the possibility of detection of the anomaly during life? The answer to this question is best derived from analysis of the protocols of the previously reported cases, presented in the accompanying table.

3. What general pathophysiologic implications can be drawn from the gross obliteration of the ductus arteriosus and the partial closure of the foramen ovale in anomalous drainage of the pulmonary veins into the coronary sinus? Nagel first called attention to the seeming paradox in circulatory mechanics expressed by closure of the ductus arteriosus and foramen ovale. For, from the standpoint of purposive compensation in congenital heart disease, the cardiovascular functions of the infant could most efficiently be carried out by a widely patent foramen ovale and ductus arteriosus. Even at a superficial glance, on the basis of intravascular pressures, it would appear that these fetal blood passages

Symptoms in Three Reported Cases of Anomalous Drainage of the Pulmonary Veins into the Coronary Sinus *

Author	Nbarro	De Groat and Thatcher	Nagel
Age at death	5½ mo.	2 yr., 4 mo., 9 days	2 mo., 24 days
Patient	White girl	White girl	White girl
Previous symptoms	Wasting, bronchitis and edema	Malnutrition, bronchitis	Malnourishment and diarrhea
Cyanosis at birth	None	None	None
History of cyanosis	Attacks since age of 3 mo.	Attacks since age of 9 mo., with labored breathing	Not recorded
Development	Child small	Child undernourished	Child malnourished
Cyanosis on examination	Present	Present	Present
Edema	Present	Not recorded	Present
Cardiac enlargement	Increased dulness and bulging of chest on left	Dulness and bulging of chest on left	Dulness on right; enlargement confirmed by roentgen study
Murmurs	Systolic at left nipple	Not timed; at left fourth rib	Systolic
Rhythm	Gallop	Regular	Regular
Additional symptoms	Premature birth; clubbing of nails; rales	Thrill present; liver palpable; rales; pulsation in veins of neck	

* The problem of whether anomalous drainage of the pulmonary veins into the coronary sinus can be diagnosed clinically as a specific lesion remains as a challenge for the future.

should have persisted. But as it really happens in anomalous drainage of the pulmonary veins into the coronary sinus, all the aerated blood from the lesser circulation, along with the venous blood from the general system, enters the right side of the heart. From here, the bulk of the mixed blood passes into the lungs through the right ventricle and pulmonary artery. The only blood which the systemic arterial distribution apparently receives is supplied by the left side of the heart via the small foramen ovale. From a physiologic standpoint, probably no blood goes into the aorta through the grossly obliterated ductus arteriosus. In functional terms, the cardiac apparatus approaches a "one-sided heart." The volume and pressure of the blood in the peripheral circula-

tion must be far below those in the pulmonary system. Of interest in this respect is the underdevelopment of patients suffering with this anomaly.

In regard to postnatal obliteration of the ductus arteriosus, various theories have been advanced. Following the traditional view of a sudden change in circulatory mechanics after birth, dependent on abandonment of the placental circulation and opening of the pulmonary bed, Schantz,[2] Walkoff [2] and Linzemeir [2] postulated that a mechanically induced stretching or kinking of the duct on first respiration with slowing of the stream, thrombosis and organization accounts for closure. Roeder,[3] Fromberg [3] and Strassman [3] attributed obliteration to the presence of a fold in the aorta in the upper border of the mouth of the duct which acts as a valvular plug when pressure rises in the aorta at birth. Abbott [4] expressed the opinion that these factors must also be given primary consideration: (1) lowering of the mean blood pressure (aortic and pulmonic pressure) in the duct and (2) contraction of its relatively muscular wall. Nagel [1c] stated the belief that obliteration of the ductus arteriosus in anomalous drainage of the pulmonary veins into the coronary sinus supports the theory of Walkoff [2] and Linzmeir.[2] In his view a low pressure in the aorta and a high pressure in the pulmonary artery after birth militate against explanations such as those of other authors.

In recent years, the dogma of a complete change in the circulation immediately after birth with rather sudden effects on the ductus arteriosus and foramen ovale (on which the conclusions in the foregoing paragraph are based) has been attacked by Patten.[5] According to his observations and speculations, obliteration of the ducts is a progressive and gradual process, similar to endarteritis obliterans and concomitant with an increase in pulmonary circulation; it may occur in the face of a high pressure in the pulmonary artery. Schaeffer [6] stated the belief that the duct gradually becomes closed by fibroelastic proliferation, along with contraction. According to Stienon,[2] occlusion is related to dilatation of the fetal isthmus. In my case the evidence may be interpreted to support the theory that obliteration of the duct is brought about by an inherent active process. There was no aortic fold. Gross obliteration

2. Cited by Abbott.[4]

3. Cited by Nagel.[1c]

4. Abbott, M. E.: Congenital Cardiac Disease, in Osler, W., and McCrae, T.: Modern Medicine, ed. 3, Philadelphia, Lea & Febiger, 1927, vol. 4, p. 762.

5. Patten, B. M., in Curtis, A. H.: Obstetrics and Gynecology, Philadelphia, W. B. Saunders Company, 1933, vol. 1, pp. 906-929.

6. Schaeffer, J. P.: The Behavior of Elastic Tissue in the Postfetal Occlusion and Obliteration of the Ductus Arteriosus (Botalli) in Sus Scrofa, J. Exper. Med. **19**:129, 1914.

had occurred in the midpart of the duct. Histologic section showed no thrombosis; the lumen remained slightly patent but contained no blood. The microscopic details of the wall were similar to those described by Schaeffer and mentioned by Patten.[5] In the hypothesis of the last author may also be sought an explanation for partial closure of the foramen ovale with a well developed, thick valvula foraminis ovalis.

4. Does embryologic or phylogenetic investigation furnish an explanation for drainage of the pulmonary veins into the coronary sinus rather than into the left atrium?

Some authors have held that the pulmonary veins arise as an unpaired trunk from capillaries at the bifurcation of the trachea and connect with the left atrium. With this view in mind, Nbarro [1a] and De Groat and Thatcher [1b] expressed the belief that in the anomaly under discussion the aperture of the common pulmonary trunk, instead of adhering to and opening into the back of the left auricle, made its attachment a little lower down and thus formed an opening into a part of the sinus venosus which normally is converted into the coronary sinus.

On the other hand, it has been shown in recent times that in dipnoeans, amphibians, reptiles, pigs and cats the common pulmonary vein opens first into the sinus venosus. According to Goette,[7] Flint,[3] Federow [3] and Schornstein,[3] this vein is an outgrowth of the sinus venosus and establishes communication with the vascular plexuses of the embryonic lung. His,[7] Born [7] and Brown [8] stated the opinion that it is a specialized part of the splanchnic venous plexus which opens into the sinus venosus.

Only later the common pulmonary vein shifts into the left atrium. According to Brown,[8] it connects with the sinus venosus first in the cephalic aspect in the median line, at a level cephalad to and between the ducts of Cuvier.

> With the displacement of the sinus venosus caudad and to the right due to inequality of growth of the two halves of the sinus and auricle, the pulmonary orifice moves only slightly to the right and empties into the left portion of the sinus to the left of the sinus valve and at a level below the septum superius. The formation of the interauricular septum by fusion of the left sinus valve with the dorso-caudal extremity of the septum superius definitely assigns the pulmonary vein to the left auricle.[8]

Davies and MacConaill [9] claimed that the transference of the opening of the pulmonary vein to the left atrium is the work of the "pulmonary

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7. Cited by Brown.[8]

8. Brown, A. J.: The Development of the Pulmonary Vein in Domestic Cat, Anat. Rec. **7**:299, 1913.

9. Davies, F., and MacConaill, M. A.: Cor Biloculare, with a Note on the Development of the Pulmonary Veins, J. Anat. **71**:437, 1937.

fold." Subsequently, by division, two and then four right and left veins develop. As the left atrium grows, these are successively taken up in its wall.

According to the embryologic descriptions just given, it seems most reasonable to assume that in anomalous drainage of the pulmonary veins into the coronary sinus the common pulmonary vein, instead of arising from (or terminating in) its normal position in the sinus venosus, finds connection in such a position, perhaps slightly caudad, as to be incorporated in that part of the sinus venosus which ultimately forms the coronary sinus. A defect in shift into the left atrium with attachment to the coronary sinus must also be considered.

SUMMARY

An example of anomalous drainage of the pulmonary veins into the coronary sinus which occurred in a 5½ month old boy is described. The literature on this anomaly is reviewed.

NOTE.—In the discussion on an article by P. A. Duff (Pulmonary Veins from Both Lungs Draining into Right Auricle with Persistent Foramen Ovale: Report of a Case, *J. Tech Methods* **18:** 114, 1938) published since this article was written, Palmer described 2 cases of anomalous drainage of the pulmonary veins into the coronary sinus. To and fro murmurs were heard. In the 3 month old infant there was cyanosis at birth; the ductus arteriosus was slightly patent.

ERYTHROBLASTIC (COOLEY'S) ANEMIA AND NEUROLOGIC COMPLICATIONS (STATUS DYSMYELINATUS)

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AND
I. S. WECHSLER, M.D.
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Erythroblastic anemia, a disturbance of the hemopoietic system, is a well established disease characterized by racial and familial incidence, mongoloid appearance, progressive anemia, deficiency of hemoglobin with decrease in the number of red cells but with large numbers of nucleated red cells in the circulation, leukopenia of high degree, enlargement of the spleen and slight enlargement of the liver and destructive changes in the bones with lesions in the bone marrow. About 60 cases so far have been reported in the literature. As far as could be ascertained, in none were there neurologic symptoms. The case to be described is of interest clinically because of the signs and symptoms of an extrapyramidal disorder and histologically for the changes in the striatum and pallidum.

REPORT OF A CASE

J. V., a 10 year old boy of Italian extraction born in the United States, was admitted to the Montefiore Hospital on Feb. 4, 1932, because of anemia from which he had been suffering all his life. The parents, born in southern Italy, a brother, 18 years old, and a sister, aged 17, both born in this country, were living and well. The patient had a normal birth and development, except for measles at the age of 5 years and tonsillectomy at the age of 6. Enlargement of the spleen was first noticed in September 1929. Shortly after this edema of the legs and dyspnea appeared; the edema cleared up spontaneously in two months.

Physical Examination.—On admission the boy was pale and mentally retarded, with mongoloid facies, slanting eyes and a marked sallow, subicteric tint over the entire body. The nose was saddle shaped. The frontal and parietal bones were prominent; accentuated depressions were present in the regions of the bregma and the lambdoid fissures. The lips were kept open, disclosing protrusion of the upper teeth (fig. 1). The upper and lower incisors contained several small notches at the free margins, but there was no evidence of Hutchinson's teeth. The upper and lower mandibles were considerably thickened. The palate was narrow and highly arched. Marked arterial pulsations were visible in the neck. A systolic thrill was palpable over the right common carotid and subclavian vessels. The

From the Neuropathological Laboratory and the Neurological Division of the Montefiore Hospital.

lower ribs of the chest had a marked outward flare, and the costochondral junctions were slightly thickened. The heart was enlarged to the left. A loud systolic murmur was heard over the entire precordium. The cardiac rate was 116 beats per minute. The abdomen was prominent and distended. The liver was enlarged, reaching as far as the umbilicus. The spleen was enormously enlarged, being felt 6 fingerbreadths below the costal margin. The blood pressure was 104 systolic and 52 diastolic in the right arm and 88 systolic and 52 diastolic in the left.

Neurologic Examination.—The patient was mentally dull and apathetic. He responded slowly to questions and commands. The face was masklike. The gait was slow and somewhat rigid. During walking the hands were close to the body and lacked the normal associated movements. A pronator sign and slight hyper-

Fig. 1.—J. V.; note the mongoloid features, gaping of the mouth, protrusion of the upper teeth, masklike facies and prominence of the mandibles.

tonicity and cogwheel rigidity of the upper extremities were noted. All the deep reflexes were exaggerated, with a tendency to ankle clonus. The abdominal and cremasteric reflexes were lively. There was a Babinski sign on the right. The fundi contained large blood vessels, the veins and arteries being about equal in size. The pupils were equal and regular and responded promptly to light and in accommodation. All the other cranial nerves were normal.

Laboratory Data.—On the patient's admission the hemoglobin content was 30 per cent; the red blood cells numbered 2,200,000, platelets 330,000 and white blood cells 10,500, of which segmented polymorphonuclear leukocytes comprised 16 per cent, nonsegmented polymorphonuclear leukocytes 63 per cent, eosinophils 2 per cent, basophils 1 per cent, lymphocytes 11 per cent, monocytes 2 per cent, myeloblasts 2 per cent, neutrophilic myelocytes 3 per cent, normoblasts 5 per cent,

megaloblasts 2 per cent and erythroblasts 2 per cent. The smear revealed marked poikilocytosis, anisocytosis and macrocytosis. Occasional Howell-Jolly and Cabot bodies were found. The bleeding time was one minute and twenty seconds. The coagulation time was nine minutes. The clot retraction time was normal. The tourniquet test and the fragility test gave negative results. The Wassermann reaction of the blood was negative. The blood was group II, Jansky. The blood contained 7.8 mg. of urea nitrogen per hundred cubic centimeters, 9 mg. of uric acid and 105 mg. of sugar. The sedimentation time was twenty minutes. The cell volume was 12 per cent. The blood culture was negative on two occasions. The urine was normal. A smear of the bone marrow, except for eosinophilia, was essentially normal. Roentgen examination of the skull disclosed marked thickening of all the bones of the skull with accentuation of the cortical portions,

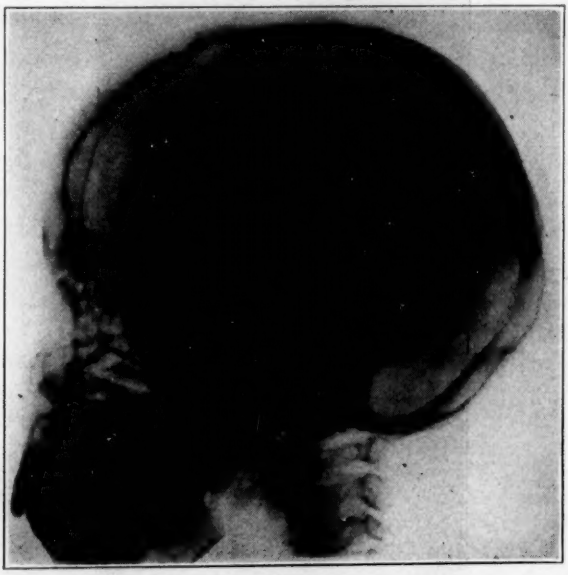

Fig. 2.—Roentgenogram of the patient's skull. Notice the marked thickening of the bones of the calvarium with accentuation of the cortical portions, which appear as a dense line, and the granular appearance of the medullary regions. There are a few spicules in the cortical portions.

which appeared as a dense white line, and a granular appearance of the medullary portions. The suture lines were also markedly accentuated. A few spicules were noted in the cortical portions (fig. 2). The cortices of all the other bones were extremely thick. The medullary portions were widened and translucent and disclosed trabeculations. There was considerable bowing of the metacarpal bone and all the phalanges. The trabeculations were most exaggerated at the ends of the radius and at the lower end of the femur. The lower dorsal and the lumbar part of the spine showed a somewhat granular appearance of the bodies of the vertebrae.

Course.—Throughout his stay in the hospital the patient had an almost continuous fever, with the temperature rising to 103 F.; at times it was about 100. In

spite of intensive therapy with liver extract and iron compounds, with numerous transfusions, the anemia failed to improve. The hemoglobin content remained at about 28 per cent and the red cell count at 1,780,000. During the episodes of sudden rises in temperature there was no evidence of any hemoclastic crisis, the urine revealing no evidence of hemoglobin or its derivatives. During the ten months in the hospital the patient gained 9 pounds (4.1 Kg.). He had a playful disposition and was able to walk in spite of his anemia. Results of neurologic examination remained unchanged.

The child was discharged from the hospital on December 10 as improved and was readmitted on April 20, 1933, because of the severe anemia and dyspnea. The examination gave essentially the same results as during the first admission. The laboratory data on the second admission disclosed that the red blood cell count was 970,000, the hemoglobin content 25 per cent and the white blood cell count 4,800, with marked anisocytosis and poikilocytosis, polychromophilia and basophilia. The blood contained urobilin (2 plus) and 0.8 mg. of bilirubin per hundred cubic centimeters. The blood urea amounted to 6 mg. per hundred cubic centimeters.

The boy received two transfusions. After the first the red cell count rose to 1,460,000. The second was accompanied by a transient reaction followed by a rise in temperature to 105.4 F., with general toxic symptoms rapidly culminating in death.

Autopsy.—A detailed description of the organs, except for those of the central nervous system, will be omitted.

General Gross Examination: The spleen was considerably increased in size and extended in an oblique line from the left costal margin to a point about 2 inches (5 cm.) below the umbilicus. It weighed 725 Gm. (normally at the age of 12 years it weighs 90 Gm.) and measured 20.5 by 10.5 by 7 cm.; it was violaceous, firm, rubbery and elastic. The lower margin of the right lobe of the liver extended to the right anterior superior iliac spine. The left lobe of the liver occupied the epigastrium; below, it extended to the umbilicus and above, to the left parasternal line meeting the spleen. It weighed 1,420 Gm., measuring 22 by 18 by 6 cm., and it cut with normal resistance. The markings were obliterated by the brownish yellow color of the parenchyma, which was probably due to hemosiderosis. The kidneys were slightly enlarged and pale. The parenchyma had a yellowish tinge. The adrenals showed no abnormality. A moderate number of petechiae, varying in size from that of a pinpoint to that of a pinhead, were scattered in the mucosa of the stomach. The calvarium was thickened, measuring in the occipital and frontal regions 9 mm. and in the parietal region about 6 or 7 mm. This increase was due to thickening of the medullary portion, which was traversed by numerous fine trabeculations. The intervening marrow was hypoplastic and brownish red. The inner and outer plates measured 1 mm. or less. The skull, like the ribs and vertebrae, was exceedingly fragile. The medulla of the ribs had the same appearance as that of the calvarium. The bodies of the vertebrae were chocolate brown, with prominent trabeculations. The long bones were not removed.

General Microscopic Examination: The liver disclosed parenchymatous degeneration. The Kupffer and polygonal cells contained a considerable amount of brownish yellow pigment. The hepatic cells of the outer third of the lobules contained considerable iron, in contrast to the rest of the lobule, which indicated the presence of several types of blood pigment. There was no evidence of myeloid metaplasia. Extensive fatty degeneration of the liver cord cells was also present. In the spleen there was congestion of the sinusoids. The endothelial cells were

prominent and contained a slight amount of blood pigment or iron. The malpighian bodies were atrophic. There was diffuse hyperplasia of the reticulum cells. The latter contained a slight amount of iron in their cytoplasm. Scattered throughout the reticulum were moderate numbers of eosinophilic myelocytes.

Deposits of blood pigment and iron were observed in other organs, such as the pancreas, kidneys, testes and various lymph nodes. The aorta gave a positive reaction for iron.

Gross Examination of Central Nervous System: The brain weighed 1,120 Gm.; it was slightly elongated in the anteroposterior direction and was markedly anemic.

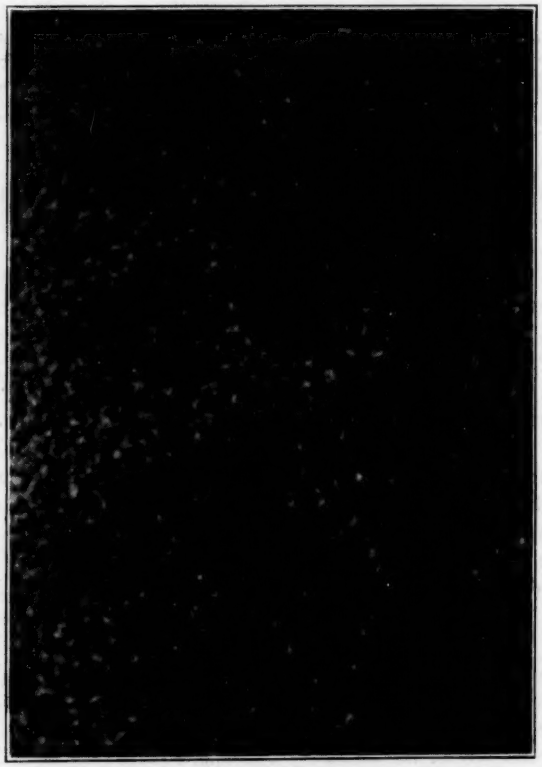

Fig. 3.—Accumulations of pigment surrounding glia and ganglion cells. Cresyl violet stain; × 500.

Sections from the cortical convolutions, basal ganglions, substantia nigra, dentate nucleus, medulla oblongata and spinal cord were embedded in celloidin and stained by the myelin sheath and cresyl violet methods. Part of the basal ganglions was stained with the Spielmeyer, sudan III and Holzer methods.

Microscopic Examination of Central Nervous System: The cortical sections of the brain, stained by the myelin sheath and cresyl violet methods, showed nothing of note.

Sections through the anterior commissure disclosed, in the myelin sheath preparation, pallor of the globus pallidus. With higher power magnification, the myelin sheath fibers within the globus pallidus stained poorly, but disintegration

of the myelin sheath could not be demonstrated. The putamen, in the same preparation, showed nothing of note. In the cresyl violet preparation, most of the larger and smaller ganglion cells within the putamen appeared normal; but some, especially the larger ones, were disintegrated and showed chromatolysis and neuronophagia. The same was true of the nerve cells of the globus pallidus. Calcific deposits were noticed around some of the vessels. Deposits of pigment surrounding glia and ganglion cells were observed in the caudate nucleus, putamen and pallidum (fig. 3). In places these accumulations of pigment granules contained large pale oval glia cells, the Alzheimer glia cells (fig. 4).

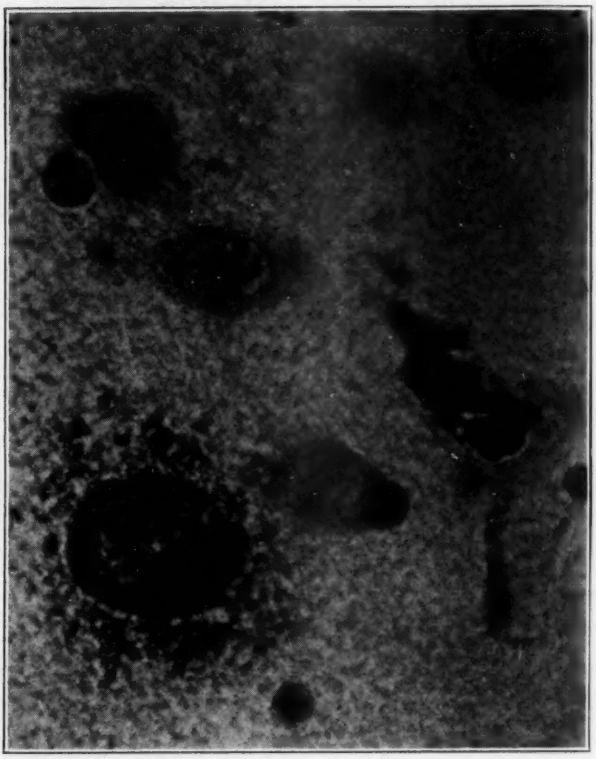

Fig. 4.—Large Alzheimer glia cell surrounded by pigment granules. Notice also the smaller pale Alzheimer glia cells. Cresyl violet stain; × 500.

In sections through the middle of the globus pallidus, there was marked demyelination of the globus pallidus, especially of the inner segment (fig. 5). With higher magnification, it was seen that the myelin fibers within the globus pallidus stained poorly and were slightly swollen and disintegrated. In the cresyl violet preparation, the ganglion cells of the striatum and pallidum showed the changes already described. Alzheimer glia cells and pigmentary deposits were noted within the putamen. In sections further down through the beginning of the red nucleus, the same process was noted in the pallidal segments. In the sudan III preparation, scattered lipoid deposits were observed in the structures just men-

tioned. Occasional perivascular accumulations of compound granular corpuscles were also noted. Proliferation of glia fibers could not be demonstrated in the Holzer preparation. The sections through the substantia nigra showed a poorly stained capsule of the red nucleus. The ganglion cells of the substantia nigra were normal but were devoid of pigment granules. In sections through the fourth

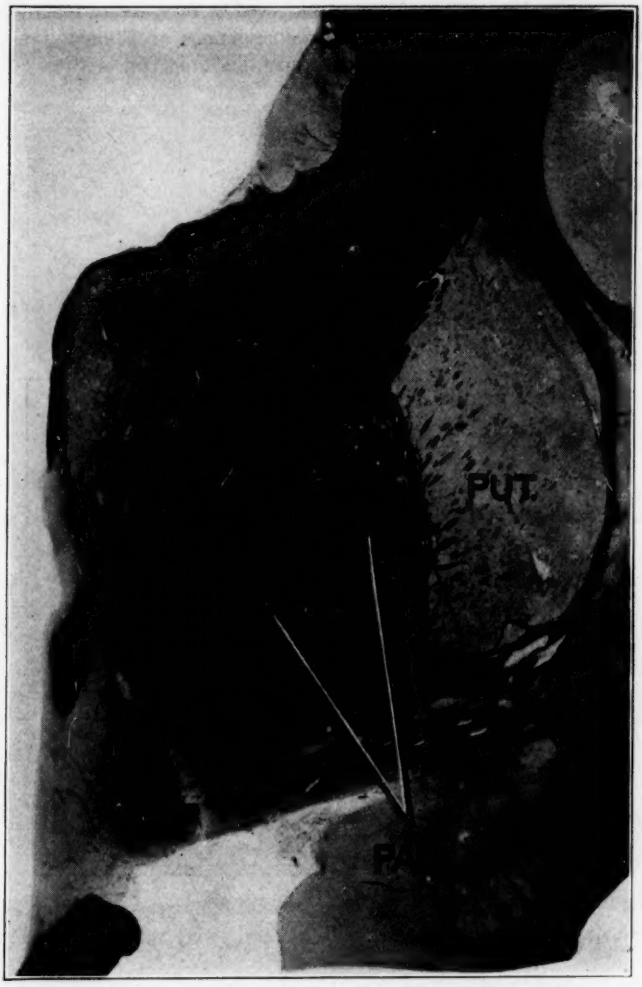

Fig. 5.—Status dysmyelinatus of the globus pallidus (*PALL.*), especially the inner segment.

ventricle, the ganglion cells of the locus caeruleus were also devoid of pigment granules. The nerve cells of the arcuate nucleus stained normally. The sections of the cerebellum and the dentate nucleus showed no abnormalities.

In the spinal cord, Helweg's tracts stained poorly and showed occasional disintegration of single myelin fibers.

The microscopic diagnosis was status dysmyelinatus secondary to erythroblastic anemia.

COMMENT

Erythroblastic anemia, first described by Cooley and his associates [1] in 1927, has received considerable attention in the literature. In none of the cases reported, however, were neurologic manifestations present. The cause of this disorder is obscure. The disease, which may be familial, occurs in infants of southern Italians and in Greeks. Many observers are of the opinion that the southern Italians with this disease are partly of Greek origin. During the height of the so-called Greek era of civilization, particularly during the reign of Alexander the Great, there was extensive colonization of all the Mediterranean countries by Greece.

The case described in this presentation conformed clinically to Cooley's case and subsequently reported cases of erythroblastic anemia. The neurologic findings, such as the masklike facies, lack of associated movements, pronator sign, hypertonicity and cogwheel rigidity, are indicative of lesions in the extrapyramidal system. The status dysmyelinatus of the globus pallidus, the pigmentary deposits about the ganglion and glia cells of the pallidum and striatum and the Alzheimer glia cells were undoubtedly responsible for the extrapyramidal symptoms. The loss in the usual pigment of the nerve cells of the substantia nigra and locus caeruleus most likely played no part in the causation of neural signs.

The pathologic changes in the striatum and pallidum in this instance were somewhat analogous to those seen in hepatolenticular degeneration (Wilson's disease and pseudosclerosis). Association of disease of the liver with that of the lenticular nuclei has recently been demonstrated not only in Wilson's disease but in many types of cirrhosis and yellow atrophy of the liver and in tumorous, vascular and other hepatic disorders. In many of these reported cases the Alzheimer glia cells and pigmentary deposits were seen in association with necrotic foci, honeycomb appearance, glial proliferation, hyalinization of the vessels, diffuse edema and degeneration of the ganglion cells.

It is difficult to state whether the simultaneous involvement of the liver, striatum and pallidus is caused by the action of a direct toxic substance produced outside of the liver, by some products of metabolism which escape detoxication in the liver or by the lack of certain metabolic substances which act directly on the nervous system. Some observers suggested that the basal ganglions regulate the function of the liver.

1. Cooley, T. B.; Witwer, E. R., and Lee, P.: Anemia in Children, with Splenomegaly and Peculiar Changes in the Bones: Report of Cases, Am. J. Dis. Child. **34**:347 (Sept.) 1927.

After the production of hepatic damage by ligation of the common bile ducts and the pancreatic ducts of dogs, Okada [2] and later Crandall and Weil [3] produced widespread spongy necrosis of the nervous tissue, active proliferation of glia cells with formation of large round and oval nuclei and diffuse changes of nerve cells, with a predilection for the deep cortical layers and the striatum. The authors maintained that the toxic substances liberated in the serum by the ligation of the common bile duct are eliminated through the choroid plexus or through the walls of the cerebral vessels, the toxic effect being most pronounced at the place of elimination and at the point of highest concentration. This explanation appears reasonable. Disease of the liver in our case possibly permitted the liberation of these toxins, which, as in Wilson's disease, have a special affinity for the striatum and in this particular instance for the pallidum also.

Of interest is the absence of a picture of subacute combined degeneration of the spinal cord despite the severe anemia. A careful scrutiny of the reported cases of Cooley's anemia disclosed the complete absence of any neural signs referable to the spinal cord.

SUMMARY

A case of erythroblastic (Cooley's) anemia with neurologic symptoms of an extrapyramidal syndrome is presented.

Histologically, there were status dysmyelinatus of the globus pallidus with pigmentary deposits, Alzheimer glia cells and changes in the nerve cells of the striatum and pallidum.

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2. Okada, S.: Ueber Veränderungen der Nervenzellen, besonders ihrer Nissl-schen Körperchen und ihres Golgischen Apparates, die durch Gallenstauung hervorgerufen werden, Okayama-Igakkai-Zasshi **43**:819, 1931.

3. Crandall, L. A., Jr., and Weil, A.: Pathology of the Central Nervous System in Diseases of the Liver: Experiments with Animals and Human Material, Arch. Neurol. & Psychiat. **29**:1066 (May) 1933.

Progress in Pediatrics

PERFORATION OF THE GASTROINTESTINAL TRACT OF THE NEWBORN INFANT

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The medical literature has many excellent case reports and several good treatises on perforation of the gastrointestinal tract of the newborn infant, but the articles are scattered in specialized journals, or the cases are listed under such obscure titles in the indexes (peptic ulcer, fetal peritonitis, melena neonatorum, pneumoperitoneum or meconium peritonitis) that it is a tedious procedure even to locate the references. I have attempted to bring together in the accompanying table all of the cases of spontaneous perforation regardless of cause, but in view of the varied approaches to the condition 1 or more cases may have been overlooked. Cases of perforation associated with definite obstruction of the bowel, intrinsic or extrinsic, are not included; cases of intrauterine rupture of the appendix have also been omitted (Abt,[1] Jackson,[2] Hill and Mason [3]).

Perusal of the literature also revealed that authors differed in their interpretations of what constitutes a rupture. In some series are included cases of ulceration through the layers of the bowel, whether or not the serosa was finally penetrated. In others are included only the cases of rupture into the free abdominal cavity. As various degrees of ulceration may occur and as microscopic sections would be necessary to enable one to determine the exact extent of involvement in some instances, it has seemed logical to classify as cases of perforation only those in which the lesion actually perforated the entire wall, including the serosa. However, all such cases even though the perforation was walled off and not associated with general peritonitis, are included.

The original purpose of limiting the study to newborn infants has not been adhered to slavishly. Only newborn patients are listed in the

From the Pediatric Department of the Hospital for Children.

1. Abt, I. A.: Fetal Peritonitis, M. Clin. North America **15**:611, 1931.

2. Jackson, F. W.: A Case of Prenatal Appendicitis, Am. J. M. Sc. **127**:710, 1904.

3. Hill, W. B., and Mason, C. C.: Prenatal Appendicitis with Rupture and Death, Am. J. Dis. Child. **29**:86 (Jan.) 1925.

Case	Author	Date	Age	Sex	Maternal History	Symptoms	Operation	Location and Size of Ulcer	Cultures	Postmortem Observations and Comment
						I. Stomach				
1	Siebold [4]	1825	2 days	..	Birth 6 weeks premature	Weakness; feeble cry	No	Lesser curvature; size of penny	No	Infant atrophic; congestion of lungs; gangrenous rupture on lesser curvature
2	Busch, G.: J. d. prakt. Arznk. u. Wundarznk. **83**: 123, 1836	1836	4 days	M	Second child	Vomiting, obstipation, blood by rectum, collapse	No	Greater curvature, anterior wall near pylorus; size of penny	No	Perforation peritonitis acute; stomach wall injected; mucous membrane of rest of gastrointestinal tract normal
3	Binz, C.: Berl. klin. Wchnschr. **15**: 148, 1865	1865	11 days	F	Fourth child	Diarrhea starting third day; distention, collapse	No	Greater curvature, anterior wall	No	Round perforating ulcer; area about it reddened; inflammation of rest of bowel
4	Ritter, H.: Arztl. Mitth. a Baden **36**: 15, 1882; cited by Dunham and Goldstein [12]	1882	12 hr.	F	.....	Blood in vomitus	No	Anterior wall	No	Cited by Dunham
5	Cade, A.: Rev. d. mal. de l'enf. **16**: 57, 1898	1898	2 mo.	M	.....	Vomiting, diarrhea, distention, collapse	No	Posterior wall near pylorus	No	Punched-out ulcer; some cellular infiltration; walled off abscess formed over pancreas; rest of stomach normal
6	Bisset, A. G.: Lancet **2**: 78, 1905	1905	45 hr.	M	Ninth child	Blood in stool profuse; born in state of semi-collapse	No	Posterior wall near cardia	No	Punched-out ulcer, adhesions about it
7	Lee, W. E., and Wells, J. R.: Ann. Surg. **78**: 36, 1923	1923	10 days	M	Negro twins	Vomiting, obstipation; roentgen study showed pyloric obstruction	Yes; patient died in 12 hr.	Greater curvature, 4 cm. from pylorus	No	No generalized peritonitis; perforation walled off; no inflammatory reaction in wall of ulcer; mass of adhesions about pylorus
8	Butka, H. E.: J.A.M.A. **89**: 198 (July 16) 1927	1927	6 days	F	First child; asphyxia	Third day fever 102.6 F.; vomiting, blood in stool, distention	No	Greater curvature, 1.5 cm. below cardia	No	Perforation peritonitis acute; air in peritoneum; blood clots
9	Stern, M. A.; Perkins, E. L., and Nessa, N. J.: Journal-Lancet **49**: 492, 1929	1929	4 days	..	Third child	Second day vomiting, distention, grunting respiration; roentgen study showed ulcer and pneumoperitoneum	Yes; patient died	Lesser curvature, posterior wall near pylorus; ¼ inch in diameter	No	Ulcer ¼ inch in diameter; partly open at autopsy; perforation peritonitis; little inflammation about ulcer
10	Selinger [47]	1932	3 mo.	M	.....	Failure to gain; difficulty in feeding	Gastrojejunostomy	Posterior wall	No	Ulcer walled off; patient recovered after operation
11	Selinger [47]	1932	11 mo.	M	.....	Blood in vomitus; collapse	No	Anterior surface	No	Infant marasmic; author suggested infection as cause
12	Dunham and Goldstein [12]	1934	21 days	M	Toxemia; cesarean section	Fever fourth day; vomiting, distention, edema; roentgen study showed pneumoperitoneum	On 13th day; patient lived 8 days	Greater curvature	B. coli in blood; 7 cultures	Pneumonia; localized abscesses; partial obstruction of sigmoid; no free fluid; pus in pockets
13	Dunham and Goldstein [12]	1934	5 days	M	Premature birth	Harelip, cleft palate, vomiting, distention; roentgen study showed no free air	No	1.5 cm. below esophagus	B. coli in blood and heart blood	Perforation peritonitis

14	Smythe, F. W.: Am. J. Surg. **24**: 818, 1934	1934	6 days	F	Negro; rheumatic heart disease; nephritis; premature birth	Vomiting and distention	No	Posterior wall, greature curvature, lower portion	No	Hypertrophied pyloric muscle; partial obstruction ileocecal valve
15	Smythe, F. W.: Am. J. Surg. **24**: 818, 1934	1934	6 days	M	Negro	Vomiting, distention, fever	Yes; patient died in 9 hr.	Just proximal to pylorus; small	No	
16	Tow, A., and Ross, H.: J. A. M. A. **111**: 1178 (Sept. 24) 1938	1938	3 days	M	Second child; normal	Fever, cyanosis, labored respiration; distention third day	No	Anterior wall; large	No	Exudative peritonitis; congestion of liver and spleen
						II. Duodenum				
1	Bourrus, J.: J. de méd. de Bordeaux **19**: 413, 1890	1890	36 hr.	F	Forceps delivery; asphyxia	Moribund, resuscitated; melena	No	1 cm. below pylorus; 6 mm. in size	No	Perforation peritonitis; rest of bowel congested; mucous membrane of ileum hyperemic
2	Gallos, P.:† De l'ulcére du duodenum, Thesis, Paris, 1912-1913, p. 143	1890	2 days	..	Long difficult labor; asphyxia	Asphyxia; melena second day	No	1 cm. below pylorus; 6 mm. in diameter	No	No peritonitis; small intestine markedly injected and mucosa hyperemic; mesentery congested; colon injected
3	Perry, E. C., and Shaw, L. E.: Guy's Hosp. Rep. **50**: 171, 1898	1898	3 mo.	F	.....	Vomiting, blood in stool, diarrhea	No	Posterior wall near pylorus; 2 ulcers	No	No generalized peritonitis; punched-out ulcer through all layers, walled off by adhesions; some free fluid in abdomen
4	Genrich:† Thesis, Paris, Gandy, 1898-1899; cited by Gallos	1898 1899	21 hr.	..	Long labor	Vomiting, melena	No	1.5 cm. below pylorus; ¾ of circumference involved	No	Ecchymosis of liver and bowel; oval ulcer of duodenum covering ¾ of circumference; complete perforation size of lentil; cited by Gallos
5	Adriance, V.: Arch. Pediat. **18**: 277, 1901	1901	10 mo.	M	.....	Vomiting, pain, diarrhea, blood in stools	No	Posterior wall just below pylorus; 1 by 2 cm.	No	Ulcer adherent to pancreas, perforating but walled off; some blood in stomach
6	Borland [38]	1902	8 mo.	M	.....	Eczema, infection; blood in vomitus; edema	No	Posterior wall just below pylorus	No	No generalized peritonitis; fibrinous exudate over pancreas, large blood clot in lesser sac; purulent vesicles on scalp
7	Samiac:† Toulouse méd. **7**: 195, 1905; cited by Gallos	1905	3 mo.	F	Postpartum phlebitis	Did not thrive; marasmus, collapse, dyspnea, fever, convulsions	No	Just below pylorus; 2 ulcers	No	Purulent peritonitis; punched out ulcers; cited by Gallos
8	Helmholz [8a]	1908	6 wk.	M	Twins	Diarrhea, loss of weight, collapse, marasmus	No	Near pylorus; 2 ulcers 3 mm. in size	No	Perforation peritonitis; punched-out ulcers; mucosa intact up to ulcer
9	Helmholz [8a]	1908	7 wk.	M	.....	Diarrhea, subnormal temperature, marasmus	No	Posterior wall near pylorus; 1.5 cm.	No	Localized peritonitis, walled off by adhesions; mucosa intact up to ulcer
10	Helmholz [8b]	1909	1 mo.	F	.....	Vomiting since birth, tarry stools, collapse	No	Pars horizontalis	No	Perforation peritonitis, purulent
11	Finny, C. E.: Proc. Roy. Soc. Med. (Sect. Stud. Dis. Child.) **2**: 67, 1908-1909	1909	10 wk.	M	First child	Vomiting, blood in stools; patient refused food, lost weight, collapsed	No	Posterior wall 2 in. from pylorus	No	Hyperplasia of pyloric muscle; no general peritonitis

Perforation of the Gastrointestinal Tract of the Newborn—Continued

Case	Author	Date	Age	Sex	Maternal History	Symptoms	Operation	Location and Size of Ulcer	Cultures	Postmortem Observations and Comment
12	Birk, cited by Helmholz [8b]	1909	6 wk.	..	.....	Gradual loss of weight from birth; sudden collapse	No	Duodenum	.....	Report cited by Helmholz as unpublished
13	Griffith, J. P. C.: New York M. J. **94**: 572, 1911	1910	6 mo.	M	.....	Vomiting, blood in stools; failure to gain; collapse	No	Posterior wall just below pylorus; 5 mm. in diameter	No	Walled off; round punched-out ulcer; also evidence of acute hemorrhagic nephritis
14	Ribadeau-Dumas, L., and Lévi-Franckel, G.: Bull. et mém. Soc. anat. de Paris **86**: 585, 1911	1911	6 mo.	M	.....	Vomiting, cyanosis, distention	No	Posterior wall 3 cm. from pylorus	No	Purulent peritonitis
15	Woods:† Thesis, Paris, Gandy, 1898-1899; cited by Gallos	1912	36 hr.	..	Healthy parents	Hematemesis and melena	.....	Posterior wall; 1 cm. in diamete:	No	Punched-out round ulcer, perforated in 2 small openings; marked reaction in peritoneal cavity; cited by Gallos
16	Entz, 1908, cited by	1912	6 wk.	..	.....	.....	.....	.....	.....	No details given except that
17	Flesch [55]		to 6 mo.							2 ulcers were perforated
18	Schmidt [39]	1913	4½ mo.	F	.....	Otitis media, distention, edema	No	3 mm. from pylorus; 3 mm. in diameter	No	Perforation peritonitis acute; swollen Peyer's patches
19	Meyer, O.: Berl. klin. Wchnschr. **50**: 1730, 1913	1913	6 wk.	..	.....	.....	No	Pars horizontalis	.....	Perforation peritonitis
20	Holt [19]	1913	3 mo.	F	Ninth child	Vomiting since age of 2 weeks; not thriving	No	Posterior wall just below pylorus	Streptococci in heart blood and lungs; streptococci and B. coli in peritoneum	Turbid fluid in abdomen; peritoneum and omentum congested; small petechial hemorrhage; punched-out ulcer, edges sloping; no inflammatory reaction
21	Nuzum, T. W.: Wisconsin M. J. **15**: 111, 1916	1916	24 hr.	..	.....	Blood in stools	No	Duodenum	No	Old adhesions to gallbladder; author suggested septic thrombosis as cause
22	Thiele [64]	1919	2 mo.	..	Normal	Vomiting since age of 3 weeks	No	Duodenum; 1 ulcer perforated, others present	.....	No generalized peritonitis; adhesions to pancreas
23	Wurm, H.: Ztschr. f. Kinderh. **43**: 286, 1927	1927	7 wk.	M	.....	Cyanosis and collapse	No	Duodenum	No	Perforation peritonitis; bronchopneumonia; cystic degeneration of pancreas
24	Somerford, A. E.: Lancet **1**: 1015, 1930	1930	14 days	M	.....	Vomiting, obstipation, distention, collapse	No	1 cm. from pylorus; small	No	Perforation peritonitis
25	Harrison [20]	1931	10 wk.	F	.....	Ophthalmia neonatorum, fever, distention, edema	Yes; ulcer not found; patient died 1 day later	Posterior wall above papilla; ½ inch in diameter	Peritoneum, B. coli, B. welchii, gram-positive cocci	Perforation peritonitis

26	Brockington, C. F., and Lightwood, R.: Lancet **2**: 1209, 1932	1932	14 days	M	Sixth child	Vomiting; gangrenous spots on groin and neck; roentgen study showed delay at pylorus	No	Junction of first and second part; 2 by 4 mm.	No	Perforation walled off; infarcts in lung
27	Moody, E., and Howard, W. M.: J. Missouri M. A. **30**: 494, 1933	1933	11 days	M	Third child	Vomiting, diarrhea, distention, collapse	No	First part; 1.5 cm.	No	Perforation walled off; no generalized peritonitis
28	Seinsheimer, F.: J. A. M. A. **105**: 875 (Sept. 14) 1935	1935	4 days	M	Placenta praevia; cesarean section	Vomiting, icterus, edema, shock, discoloration of lower part of abdomen	No	Second part; small	No	Perforation peritonitis; thick creamy fluid, congestion; microscopic study
29	Heijbroek, N. I.: Nederl. tijdschr. v. geneesk. **79**: 4443, 1935	1935	Newborn	..	Fifth child; premature birth	Blood in vomitus; collapse	No	Duodenum	No	
30	Thelander and Mathes [21]	1939	12 days	F	Second child	Vomiting, distention, edema; roentgen study showed pneumoperitoneum	Yes; child died in 12 days; sulfanilamide given	Duodenum; long tear	B. coli in blood; B. coli and streptococci in peritoneum	Perforation peritonitis, empyema
						III. Bowel				
1	Breslau: Monatschr. f. Geburtsh. (supp.) **21**: 141, 1863; Schmidt's Jahrb. **121-122**: 187, 1864	1863	Newborn	..	.....	Child stillborn; had hydrocephalus and other anomalies	No	Ascending colon; 2 small perforations	No	Hydrocephalus
2	Zillner [33]	1884	15 hr.	M	Normal birth	Cyanosis, obstipation	No	8 mm. tear in sigmoid	No	Perforation peritonitis, ecchymosis
3	Zillner [33]	1884	15 hr.	F	Normal birth	Obstipation	No	17 cm. above anus; 1 to 2 cm. in diameter	No	Perforation peritonitis
4	Zillner [33]	1884	12 hr.	F	Birth at term	Distention, obstipation	No	Sigmoid; half of circumference torn	No	Perforation peritonitis; gas, ecchymosis
5	Zillner [33]	1884	13 hr.	M	.....	Distention, obstipation	No	Sigmoid	No	Perforation peritonitis, ecchymosis
6	Orth [14]	1887	.....	..	.....	.....	No	.....	.....	Perforated Meckel's diverticulum
7	Dubler [10]	1888	5 days	M	.....	.....	No	Large bowel; cyst with meconium	No	Sepsis, endocarditis, meningitis; large cyst attached to bowel containing meconium from perforation
8	Paltauf [31]	1888	2 days	M	Normal birth	Child found dead in crib	No	2 ruptures in large bowel; 18 mm. in diameter	No	Perforation peritonitis
9	Paltauf [31]	1888	15 hr.	M	Normal birth	Cyanosis, edema	No	Transverse colon; 1 cm. in diameter	No	Perforation peritonitis
10	Paltauf [31]	1888	1 day	F	Normal birth	Sudden death	No	3 ruptures in sigmoid; 1 cm. long	No	Perforation peritonitis
11	Paltauf [31]	1888	1 day	M	Normal birth	Collapse	No	Multiple ruptures in bowel	No	Perforation peritonitis

Perforation of the Gastrointestinal Tract of the Newborn—Continued

Case	Author	Date	Age	Sex	Maternal History	Symptoms	Operation	Location and Size of Ulcer	Cultures	Postmortem Observations and Comment
12	Paltauf [81]	1888	15 hr.	F	Normal birth	Cyanosis, obstipation	No	Transverse colon	No	Perforation peritonitis
13	Tolmatschew: Verhandl. d. internat. Med. Cong. (1890), 1891, vol. 2, pt. 6, p. 67	1890	3 days	..	Not known	Pathologic specimen	.....	Small intestine, opposite mesentery; 3 by 1 mm.	No	Serosa thickened, fibrinous adhesions about opening; Peyer's patches and solitary follicles sharply demarcated; lesion believed to be syphilitic gumma
14	Genersich [13]	1891	45 hr.	M	Normal birth	Cyanosis, distention	No	Ileum	No	Perforation peritonitis
15	Falkenheim and Askanazy, M.: Jahrb. f. Kinderh. **34**: 71, 1892	1892	21 days	F	Premature birth	Cyanosis, distention	No	Splenic flexure	No	Perforation peritonitis, adhesive type
16	Shukowski [16]	1902	4 days	..	.....	Vomiting, diarrhea, distention, edema, obstipation, collapse	No	Junction of jejunum and ileum; size of pea	No	Believed to be rupture of Meckel's diverticulum with perforation peritonitis
17	von Sury, K.: Vrtljschr. f. gerichtl. Med. (supp. 2) **43**: 91, 1912; cited by Rudnew [17]	1912	24 hr.	M	Normal birth	Obstipation	No	Sigmoid; 3 cm. slit	No	Perforation peritonitis
18	Rudnew [17]	1915	Newborn	M	Premature birth; postpartum fever; hydramnios	Infant stillborn; distention	No	Small bowel; irregular, 1.5 cm. long	No	Perforation peritonitis microscopic sections of perforation; meconium stasis, necrosis
19	Rudnew [17]	1915	4 days	M	Normal birth	Not given	No	Transverse colon	No	Perforation peritonitis; atelectasis of lungs
20	Spies, P.: Inaug. Dissert., Heidelberg, 1917	1917	Newborn	M	Postpartum fever	Infant stillborn, macerated, edematous	No	Transverse colon	No	Perforation peritonitis
21	Russell [63]	1927	3 days	F	Normal birth	Obstipation, cyanosis and distention starting on third day	Yes; patient died in 4½ hr.	Cecum; linear tear 1 inch long	No	Perforation peritonitis
22	Fischer [11]	1928	18 hr.	..	Normal birth	Vomiting, obstipation, cyanosis, distention	Yes; ulcer not found; enterostomy	Perforated diverticulum in transverse colon below splenic flexure	Streptococci from peritoneal fluid	Perforation peritonitis; excessive development of lymphoid tissue and Lieberkühn's glands; cystic degeneration of glands
23	Hunter [15]	1928	4 days	M	Toxemia; premature birth	Fever, cyanosis, distention, edema	No	Meckel's diverticulum	No	Perforation peritonitis; did not look like infectious process; long diverticulum-like nipple
24	Froboese, C.: Virchows Arch. f. path. Anat. **269**: 595, 1928	1928	1 day	M	Normal	Not given	No	Ileum	No	Fibropurulent exudate, gangrenous perforation; no cellular infiltration
25	Froboese, C.: Virchows Arch. f. path. Anat. **269**: 595, 1928	1928	Newborn	M	.....	.....	No	7 cm. above ileocecal junction	No	Perforation peritonitis
26	Froboese, C.: Virchows Arch. f. path. Anat. **269**: 595, 1928	1928	2 days	M	.....	.....	No	5 cm. above ileocecal junction	No	Perforation peritonitis
27	Froboese, C.: Virchows Arch. f. path. Anat. **269**: 595, 1928	1928	2½ days	..	.....	.....	No	Ileum	No	Chronic adhesive peritonitis

28	Salter, A. E. H.: M. J. Australia **1**: 422, 1930	1930	48 hr.	..	Normal; sixth child	Vomiting, obstipation, cyanosis; roentgen study showed obstruction	No	15 cm. from pylorus; area gangrenous	No	Perforation peritonitis; large bowel undistended
29	Boikan [9]	1930	24 hr.	F	Negro	Vomiting, cyanosis, distention, edema	No	Ileum, 60 mm. above junction with colon	No	Perforation peritonitis; excessive development of lymphoid tissue; glands of Lieberkühn enlarged; careful microscopic studies
30	Wong and Hu [6].....	1930	Newborn	M	Chinese; hydramnios	Child stillborn; dystocia due to abdominal distention	No	2.5 cm. above ileocecal valve	No	Perforation peritonitis
31	Wong and Hu [6].....	1930	1 hr.	M	Chinese; toxic fever, hydramnios; postpartum fever	Distention	No	Ileum; 2 perforations	No	Perforation peritonitis; old adhesions and calcification
32	Jachens [22]	1932	3 days	..	Normal	Vomiting, fever, obstipation, cyanosis, distention; roentgen study showed pneumoperitoneum	No	Cecum	No	Perforation peritonitis
33	Jachens [22]	1932	7 days	..	Normal	Cyanosis, distention, fever; roentgen study showed pneumoperitoneum	Yes; patient died in 1 day	Cecum	Streptococci and B. coli in peritoneum	Perforation peritonitis
34	Jachens [22]	1932	4 days	..	Normal	Vomiting, cyanosis, distention; roentgen study showed pneumoperinoneum	Yes; perforation not found; patient died in 17 hr.	Right colic flexure	No	Perforation peritonitis
35	Scott [18]	1933	4 days	M	Premature birth; placental infarcts	Vomiting, distention, edema, reddened skin over affected area	No	1 cm. from appendix	No	Perforation peritonitis; ulcerative colitis in sigmoid and colon
36	Medearis, D. N.: Am. J. Dis. Child. **45**: 114 (Jan.) 1933	1933	6 days	M	Normal	Vomiting after 36 hours, obstipation, distention, fever	Yes; patient died on sixth day	2 perforations in ascending colon	No	Perforation peritonitis; fibrinous exudate; hemorrhagic area over surface of cecum
37	de Vel [23]	1933	2 days	M	Normal	Vomiting, distention; roentgen study showed pneumoperitoneum	No	Transverse colon, middle third	No	Perforation peritonitis
38	de Vel [23]	1933	2 days	M	Normal	Vomiting, distention, cyanosis; roentgen study showed pneumoperitoneum	Yes; lesion not found	Not known	No	Autopsy not permitted
39	Markowitz, B., and Loar, R.: Am. J. Obst. & Gynec. **27**: 733, 1934	1934	20 min.	..	Injury at sixth month; rapid distention of abdomen afterward	Distention; petechiae on skin	No	Jejunum; 2 small perforations	No	Perforation peritonitis; greenish material from perforations; spleen enlarged, deep red; moderate interstitial nephritis

† The cases of Genrich, Woods and Samiac were well abstracted by Gallos, but the original articles were not available. Gallos also abstracted a case report (observation 19) without giving the name of the author, and the case is therefore included under the name of Gallos, as the original article also was not available (Bull. Soc. anat. de Bordeaux, March 10, 1890).

section of the table which concerns perforation of the bowel below the duodenum, but the process may be present in the peptic area from birth, giving symptoms for weeks or even months before it comes to a climax in rupture or peritonitis. A duodenal perforation is most likely to remain walled off, owing to the retroperitoneal course of most of the duodenal part of the bowel.

It was impossible, therefore, to draw a definite line delimiting the newborn period. Furthermore, if cases of infants months old instead of days old were left out, practically every reported series of cases would thereby be disrupted; some of the "traditional" cases have been mentioned so frequently in the past that to include them seemed less confusing than to revise the lists. No cases of children a year or more old are included.

INCIDENCE

Perforation of the gastrointestinal tract of the newborn is rare. Many pediatricians have practiced medicine the normal span of years without encountering a single case. Few doctors even with entrée to large pediatric wards and nurseries have noted the anomaly in more than 3 or 4 cases. Not all observed cases are reported, and many cases are undoubtedly missed. Autopsies on stillborn infants are still too infrequent, and even if a postmortem examination is performed and an anatomic diagnosis of peritonitis made, a pinpoint rupture is easily missed. Even an ulceration is readily passed over except in a careful examination of the entire intestinal mucosa.

Rupture has been reported as occurring in the stomach, the duodenum and the small and the large bowel. Gastric perforation is somewhat rarer than duodenal, and both occur less frequently than rupture of the rest of the bowel. There are recorded 16 instances of perforation of the stomach, 30 of the duodenum and 39 of the remaining portion of the gastrointestinal tract.

The reported cases date back to 1825, when Siebold [4] presented the first description of rupture of the stomach of a newborn child. In 1838 Simpson [5] reported a large series of cases of peritonitis in fetuses. Although he did not mention perforation, his findings suggest that it had occurred in some of the cases. His description of inflammation, written before the days of bacterial knowledge, should be read by any one reviewing the literature on fetal peritonitis with or without rupture.

The sex incidence is a little less than 3 boys to 1 girl in the cases in which the sex has been stated.

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4. Siebold, A. E.: Brand in der kleinen Curvatur des Magens eines atrophischen Kindes, J. f. Geburtsh. **5**:3, 1826.

5. Simpson, J. Y.: Notices of Cases of Peritonitis in Foetus in Utero, Edinburgh M. & S. J. **2**:390, 1838.

SYMPTOMS

A variety of symptoms have been recorded, and an attempt will be made to group them logically. An infant with perforation peritonitis present at birth or occurring soon after presents a fairly classic picture. The little patient looks sick. He is cyanotic; the respirations are rapid and grunting; the abdomen is distended, and the abdominal wall, the flanks and the scrotum or vulva are usually edematous. Frequently brawny induration of the edematous area, which may resemble erysipelas, is also present. Food is taken poorly or not at all. Vomiting is frequent and persistent. The vomitus contains bile and may contain blood. The stools are either absent or scant; some mucus or blood may be passed. The temperature may be subnormal, but varying degrees of fever have been reported. The blood count is of little or no value. The hemoglobin content may be very high, which probably indicates only dehydration. The leukocytes may or may not respond with a rise.

In cases of intrauterine perforation, the abdomen has at times been so distended at birth that delivery was impossible until paracentesis of the abdomen had been performed. Wong and Hu [6] reported 2 cases of dystocia due to fetal peritonitis with distention. Geerling [7] wrote about fetal peritonitis and hydramnios.

In other cases the presenting symptom has been melena, with blood in the vomitus, in the stool or in both, followed by collapse and death. Autopsy has then revealed perforating ulcer, usually in the stomach or duodenum.

In 1 reported case the child was found dead in the crib, although previous abnormality had not been noted. A number of the infants have been stillborn.

The infants who have survived for weeks or months have had a history of gastrointestinal disturbances either from birth or from some time preceding the perforation. Usually there has been a period of refusal of food, vomiting, loss of weight and often diarrhea. In several instances definite infection has been present, such as infected eczematous lesions or otitis media. Peptic ulcer with perforation in marasmic or athreptic infants has been stressed by Helmholz.[8]

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6. Wong, A. I. H., and Hu, C. H.: Fetal Peritonitis, China M. J. **43**:578, 1929.

7. Geerling, J. G.: Fetale Peritonitis und Hydramnion, Zentralbl. f. Gynäk. **56**:40, 1932.

8. Helmholz, H.: (*a*) Ueber Duodenalgeschwüre bei der Pädatrophie, Deutsche med. Wchnschr. **35**:534, 1909; (*b*) The Relation of Duodenal Ulcers to Atrophic Conditions of Infants, Arch. Pediat. **25**:661, 1909.

ROENTGEN EXAMINATION

A flat plate of the abdomen in a case of perforation may reveal free air in the peritoneal cavity, and if barium sulfate has been given by mouth the site of rupture may be located. Such knowledge may greatly facilitate the work of the surgeon, and the examination involves little risk to the patient. In several of the recorded cases the surgeon failed to find the tear at operation.

If the perforation is walled off and does not communicate with the peritoneal cavity, the barium sulfate meal may reveal the pathologic state either as an ulcer or as obstruction to the normal passage of the meal. In some cases a preoperative diagnosis of pyloric stenosis has been made.

PATHOLOGY

For complete individual postmortem observations readers will have to consult the original articles. Here an attempt will be made only to present the classic features and the outstanding or significant variations. Remarks will generally be limited to peritoneal and gastrointestinal data.

In the classic case of perforation peritonitis, when the abdominal cavity is opened gas and fluid escape. The fluid is stained with bile and meconium, and if food has been ingested this and other intestinal contents may be noted in the peritoneal cavity. If there has been recent perforation into a previously normal peritoneum, the bowels will be injected, congested and plastered with a fresh exudate, but there will be no dense adhesions. If the peritonitis is of slightly longer duration, firmer adhesions may be present, matting the intestinal loops to each other and to other organs of the abdominal cavity. Meconium plaques due to calcification of the escaped intestinal contents may be present. According to Boikan [9] these calcifications may occur in twenty-four hours and do not, therefore, necessarily represent an old process.

In some cases there is evidence of early, probably sterile, fetal peritonitis. The intestinal loops are bound together by dense vascular fibrous adhesions which bleed profusely if separation is attempted. The loops of bowel may also be adherent to the organs of the abdominal cavity and even to the parietal peritoneum. When this picture confronts the operator, further procedure is usually hopelessly blocked, for dissection and exploration are impossible. Even at autopsy it may be difficult to determine the exact relationship of the organs. If the perforation was still present at birth or if a fresh one occurred, there will be superimposed fresh infectious peritonitis. As will be considered in the section on etiology, a patient with early fetal peritonitis may not

9. Boikan, W. S.: Meconium Peritonitis from Spontaneous Perforation of the Ileum in Utero, Arch. Path. **9**:1164 (June) 1930.

have persistent perforation but will usually undergo operation or autopsy because the massive adhesions will almost certainly cause obstruction. The picture is different from that of fresh perforation peritonitis in a previously normal peritoneum.

As noted previously rupture is more often walled off when situated in the peptic area than when it is in the remaining portion of the bowel. If such repair has occurred, there is no generalized peritonitis, though there may be some free fluid in the abdominal cavity. Thus the picture observed at operation or autopsy depends on the site of the lesion. Frequently the pancreas is involved in the adhesions.

Dubler [10] reported a case of rupture in the lower part of the bowel which had become walled off and was diagnosed as a cyst. Microscopic sections revealed the presence of meconium in the cyst.

Fischer's [11] patient had a long diverticulum that was perforated at the tip.

An occasional patient has had a fibropurulent exudate, and some have had a dry adhesive type of peritonitis with pockets of pus.

From the gross pathologic descriptions just presented it is evident that the site of the perforation cannot always be determined at operation. If the perforation is fresh, if the relation of the loops of bowel and the organs has not been disturbed and if only a recent inflammation is present, difficulty in locating the rupture is usually not encountered. With the old fibrous type of peritonitis, failure to locate the tear is not unusual.

A lesion of the stomach is usually situated on the anterior wall of the greater curvature near the pylorus, though no part of the stomach is exempt. Most of the reported ulcers in the duodenum occurred on the posterior wall in the upper portion near the pylorus. No satisfactory explanation for these predilections has been offered.

Ruptures occur about twice as often in the large as in the small bowel. In the small bowel there seems to be a predilection for the terminal part of the ileum, but all parts of the colon are equally likely to be involved.

A single perforation occurs more commonly than multiple lesions, but two and even more in a single case have been described. The size varies from pinpoint to an almost complete tear of the intestinal wall. Frequently, particularly in the peptic area, nonperforating ulcers are also present. Ulceration of the stomach or duodenum is often described as round or oval, and a lesion of the bowel is more apt to be an irregular or elongated tear.

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10. Dubler, A.: Eine eigenthümliche Cyste in der Bauchhöhle eines Neugeborenen, Virchows Arch. f. path. Anat. **111**:567, 1888.

11. Fischer, A. E.: Fetal Peritonitis: Report of a Case Following Spontaneous Rupture of the Large Intestine, Am. J. Dis. Child. **36**:774 (Oct.) 1928.

In microscopic sections also a peptic ulcer differs from an ulcer of the bowel. Several microscopic studies of serial sections through the ruptured area have been made. Dunham and Goldstein [12] described the peptic ulcer as a punched-out crater, round or oval. The edges are sloping and not undermined. The mucosa is usually intact and normal up to the ulcer. Little or no cellular infiltration is present. At the base of the ulcer there may be evidence of an eroded or thrombosed vessel. At the site of perforation will be noted some necrotic material. Ulceration of another type has shown considerable round cell infiltration with redness and inflammatory reaction about the perforation. This is not common, and the descriptions have monotonously repeated: "No inflammatory reaction."

Rupture of the bowel has been less uniformly described. This fact may point to a greater variety of the factors contributing to perforation of the bowel. Rupture of or at the site of Meckel's diverticulum has been described by Genersich,[13] Orth,[14] Hunter [15] and Shukowski.[16] Defects in the intestinal wall with false diverticula received for a time considerable attention. Defects in the muscular layers have been described, the weakness of the wall at the site of penetrating vessels has been stressed, and developmental anomalies of the glands and lymphoid tissue have been proposed as predisposing to false diverticula of the walls (Rudnew,[17] Fischer [11]). Boikan's [9] pathologic report is the most complete, but his findings, according to his own statement, are unique and therefore not of much help in determining the cause in other cases. Boikan's patient had chronic meconium peritonitis with advanced fibrosis and calcifications. At the site of the perforation there were excessive development of lymphatic tissue and deeply penetrating crypts of Lieberkühn. The longitudinal muscle layer had almost disappeared, and there was marked thinning of the circular layer. Cystic dilatation of the glands was also noted.

Although according to the descriptions just cited rupture of the bowel differs from ulceration with perforation of the stomach or duodenum, other authors have described ulceration of the bowel with

12. Dunham, E. C., and Goldstein, R. M.: Rupture of Stomach in Newborn Infants, J. Pediat. **4**:44, 1934.

13. Genersich, A.: Bauchfellentzündung beim Neugebornen in Folge von Perforation des Ileums, Virchows Arch. f. path. Anat. **126**:485, 1891.

14. Orth, J.: Lehrbuch des speciellen pathologischen Anatomie, Berlin, A. Hirschwald, 1887, vol. 1, p. 765.

15. Hunter, W. C.: Perforated Gangrenous Meckel's Diverticulum in a Newborn Infant: Report of a Case, Am. J. Dis. Child. **35**:438 (March) 1928.

16. Shukowski, V. P.: Perforated Peritonitis in Newborn, Med. obozr. **57**:117, 1902; cited by Hunter.[15]

17. Rudnew, W.: Ueber die spontanen Darmrupturen bei Foeten und Neugeborenen, Inaug. Dissert., Basel, 1915.

rupture. Scott's [18] patient had colitis; others have had evidence of inflammation of Peyer's patches and of the solitary lymph follicles. Such inflammation may lead to rupture in typhoid, and there is every reason to assume that it may at times do so in inflammatory diseases of the newborn. This will be further considered in the section on etiology.

BACTERIOLOGY

Few bacteriologic studies have been made in the reported series. Probably it is generally assumed that the intestinal tract is contaminated by bacteria so soon after birth that cultures would reveal only these secondary invaders. Unfortunately, too, it has been assumed that rupture occurring in utero must be sterile, and culture has accordingly been neglected. Both assumptions may be incorrect.

Dunham and Goldstein [12] reported 2 cases of rupture of the stomach in which Bacillus coli was found in blood cultures. In the first case the blood culture was positive on the first day and six subsequent cultures remained positive.

Holt [19] in a case of duodenal perforation in a 3 month old infant found that the heart blood culture contained streptococci. Cultures of material taken from the lung at autopsy also yielded streptococci, and the peritoneal fluid contained B. coli and streptococci. Harrison [20] reported B. coli, Bacillus welchii and gram-positive cocci in the peritoneal fluid. My associate and I [21] found B. coli in two blood cultures, B. coli and streptococci in the peritoneal fluid and B. coli in the pleural fluid.

No blood cultures have been mentioned in reports of cases of rupture of the lower part of the bowel. In Fischer's [11] case there were streptococci in the peritoneal exudate. In Jachens' [22] case there were streptococci and B. coli in the abdominal cultures. De Vel [23] mentioned a purulent exudate but not culture.

Since the intestinal tract harbors bacteria a few hours after birth, positive cultures of material obtained from the abdominal cavity any time after delivery cannot be considered significant; but it is interesting

18. Scott, A. J.: Fetal Peritonitis, California & West. Med. **39**:410, 1933.

19. Holt, L. E.: Duodenal Ulcers in Infancy, Am. J. Dis. Child. **6**:381 (Dec.) 1913.

20. Harrison, P.: A Case of Perforated Duodenal Ulcer in an Infant, Arch. Dis. Childhood **6**:245, 1931.

21. Thelander, H. E., and Mathes, M.: Duodenal Perforation in a Newborn Infant Treated Surgically and with Sulfanilamide, Am. J. Dis. Child. **57**:596 (March) 1939.

22. Jachens, M.: Fetale Meconiumperitonitis durch Spontanperforation des Darms, Monatschr. f. Kinderh. **53**:188, 1932.

23. de Vel, L.: Intestinal Perforation with Pneumoperitoneum in a Newborn Infant, Am. J. Dis. Child. **45**:587 (March) 1933.

and probably pertinent that in the 3 cases in which blood was obtained before death all cultures yielded B. coli. It is regrettable that for none of the stillborn infants was peritoneal fluid or heart blood cultured.

ETIOLOGY

As stated earlier, perforation in association with obstruction of the bowel is fairly common. Cases of this condition are not included in the table. Boikan [9] referred to many such cases. The obstruction may be due to volvulus, atresia, congenital bands, intussusception, angulations or kinks in the bowel, herniation or other factors. The cases of meconium stasis in which there was definite obstruction have not been included in this paper; instead these cases have been placed with the cases of obstruction, as this seemed more logical. In a recent review of cystic fibrosis of the pancreas Andersen [24] classified the condition in the newborn with putty-like meconium as steatorrhea. Obstruction of the bowel by meconium has been described by Landsteiner,[25] Bullowa and Brennan,[26] Fanconi,[27] Hughes,[28] Kornblith and Atani [29] and Dodd.[30] In 1 of Rudnew's [17] cases necrosis of the bowel wall may have been associated with stasis of meconium and mucus. Both Paltauf's [31] and Pfaff's [32] cases may belong in the group in which the meconium was abnormal but obstruction was not apparent.

The theory that trauma at the time of delivery causes rupture was first proposed by Zillner [33] and has been discussed from time to time since. This explanation is not generally accepted. It is hard to imagine that a normal bowel, protected as it is by the abdominal wall and itself

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24. Andersen, D. H.: Cystic Fibrosis of the Pancreas and Its Relation to Celiac Disease: Clinical and Pathologic Study, Am. J. Dis. Child. **56**:344 (Aug.) 1938.

25. Landsteiner, K.: Darmverschluss durch eingedicktes Meconium; Pankreatitis, Centralbl. f. allg. Path. u. path. Anat. **16**:903, 1905.

26. Bullowa, J. G. M., and Brennan, R. E.: Intrauterine Intestinal Obstruction from Inspissated and Impacted Meconium, J. A. M. A. **73**:1882 (Dec. 20) 1919.

27. Fanconi, G.: Fünf Fälle von angeborene Darmverschluss: Dünndarmatresien, Duodenalstenose, Meconiumileus, Virchows Arch. f. path. Anat. **229**:207, 1920.

28. Hughes, E. E.: Acute Intestinal Obstruction Due to Inspissated Meconium, Brit. J. Child. Dis. **19**:32, 1922.

29. Kornblith, B. A., and Atani, S.: Meconium Ileus with Congenital Stenosis of Main Pancreatic Duct, Am. J. Path. **5**:249, 1929.

30. Dodd, K.: Intestinal Obstruction Due to Meconium Ileus in a Newborn Infant, J. Pediat. **9**:486, 1936.

31. Paltauf, A.: Die spontane Dickdarm Ruptur der Neugeborenen, Virchows Arch. f. path. Anat. **111**:461, 1888.

32. Pfaff, E.: Die spontane Darmruptur bei Neugeborenen, Inaug. Dissert., Giessen, von Munchow, 1899.

33. Zillner, E.: Ruptura flexurae sigmoidis neonati inter partum, Virchows Arch. f. path. Anat. **96**:307, 1884.

mobile and elastic, could be caught and blown out during the passage of the baby through the birth canal. An enema or a lavage could conceivably traumatize the tract, but in the reported cases these procedures cannot be implicated either because they were not employed or because they were used only after the onset of symptoms.

Congenital defect of the bowel has been suggested, and rupture has been reported as occurring with both true and false diverticula. This etiologic possibility has been carefully discussed by Boikan,[9] Fischer [11] and Rudnew,[17] but defect of the bowel wall will not explain spontaneous rupture in all cases.

Pathologic change in the central nervous system, particularly in the hypothalamus, has been linked with peptic ulcer by Fulton.[34] In 1 of Dunham and Goldstein's [12] cases autopsy was performed with this in mind, but no abnormality was found in the brain. In reports of the other cases there is no record of any search for such a condition.

A transitory obstruction of the blood supply to a part of the tract, either by direct interference in the vessel or by a kink or twist of the bowel, may be a more common cause of degeneration of the intestinal wall than is generally apparent at the time of study. The process of rotation increases the possibility of such an occurrence. Rotation of the bowel takes place at about the tenth week of fetal life (Dott [35]), and the structures are then extremely small and fragile. It is possible that accidents to the bowel wall may happen at this stage and that the damage may be remedied either partially or wholly by subsequent growth and development.

There is evidence that such accidents occur. A patient seen recently through the permission of Dr. Mary Mathes may serve as an illustration.

A 3 day old infant was brought to the hospital because of vomiting and obstipation since birth. The vomitus contained bile. The baby appeared in good condition; there was no evidence of infection, and there was no abdominal distention. Peristaltic waves passing across the abdomen were readily observed. A barium sulfate enema revealed a wormlike large bowel patent to the ileocecal valve. A preoperative diagnosis of atresia was made. When the abdomen was opened, however, the loops of bowel were found matted together and bound to the organs of the peritoneal cavity, as well as to the peritoneal wall, by dense, firm adhesions. There was no free fluid in the peritoneal cavity, and cultures of material taken before anastomosis was made were sterile. The condition, therefore, was old sterile peritonitis. With great difficulty the dilated bowel was traced to its union with the atrophic part, at a point about 12 inches (30 cm.) above the ileocecal valve. When the intestine was traced to its obstruction it was seen that the distended part made two loops about the atrophic part. An anastomosis was made with great difficulty because of the massive involvement. The child

34. Fulton, J. F.: New Horizons in Physiology and Medicine, New England J. Med. **207**:60, 1932.

35. Dott, N. M.: Anomalies of Intestinal Rotation: Their Embryology and and Surgical Aspects, Brit. J. Surg. **11**:251, 1923.

died twenty-four hours postoperatively. At autopsy the bowels were removed en masse after separation of dense adhesions to all the adjacent tissue. Careful dissection revealed malrotation; this did not obstruct the bowel, but about 12 inches above the ileocecal valve there was atresia of the bowel.

Logical reconstruction of this case indicates the following sequence of events: malrotation, with injury to the vessels or to the bowel wall, resulting in perforation and escape of intestinal contents, which caused sterile peritonitis; subsequent healing of the rupture, with atresia of the lumen at the site of perforation. It is conceivable that in some cases repair of the rupture does not take place or there is subsequent perforation proximal to the obstruction in the distended bowel. If this happens, infection may be superimposed on old sterile peritonitis. The picture presented in either of the cases just cited is very different from that of peritonitis due to a recent perforation.

Infection as a cause of perforation of the bowel has not been given a prominent place. In only 3 cases of the entire series was blood cultured before death, and, as noted previously, all of the cultures were positive. In 1 other case a heart blood culture was positive. Authors who have expressed the belief that intrauterine perforation peritonitis is sterile would have a more convincing argument if cultures substantiated their contentions. The role of infection in producing nonperforating peptic ulcer has been stressed by Dunham and Shelton,[36] Kennedy [37] and Holt.[19] The older infants in the series presented evidence favoring bacterial invasion as a factor; Borland's [38] patient had infected eczema, Schmidt's [39] patient had otitis media, and Helmholz' [8] patients were marasmic.

It is possible that infection also may play a role in causing perforation before or at birth. The sterility of the fetus in utero is only relative. It is generally accepted that certain diseases, such as syphilis, malaria, smallpox and typhoid, have been transmitted to the fetus via the mother's circulation. Bacterial studies have also been made of the environment of the infant just before and at delivery. Amniotic fluid cultured at cesarean section is not invariably sterile (Harris and Brown [40]). Several cultural studies have been made of placental blood,

36. Dunham, E., and Shelton, M. T.: Multiple Ulcers of the Stomach in a Newborn Infant with Staphylococcus Septicemia, J. Pediat. **4**:39, 1934.

37. Kennedy, R. L. J.: Etiology and Healing Process of Duodenal Ulcer in Melena Neonatorum, Am. J. Dis. Child. **31**:631 (May) 1926.

38. Borland, H. H.: A Case of Infantile Acute Eczema; Haematemesis; Duodenal Ulcer; Death, Lancet **2**:1084, 1903.

39. Schmidt, W.: Das Ulcus Rotundum duodeni in ersten Lebensjahr, Berl. klin. Wchnschr. **50**:593, 1913.

40. Harris, J. W., and Brown, J. H.: The Bacterial Content of the Uterus at Caesarean Section, Am. J. Obst. & Gynec. **13**:133, 1927.

cord blood and the blood of stillborn infants (Slemons,[41] Penfold and Butler,[42] Kobak [43]). A correlation has been found between the frequency of positive cultures of placental and cord blood and the length of time the membranes have been ruptured or the duration of labor. Cultures of heart blood of stillborn infants or of infants who died at birth in these instances has yielded results parallel to results of culture of placental blood. An illustrative case was recently observed in the wards of the Hospital for Children. A Japanese mother delivered a baby two days after the rupture of the membranes. At the time of birth a foul odor was noted, and for several days the mother had a slight postpartum fever. The infant breathed and cried spontaneously but did not nurse well. When she was examined, the abdomen was distended and there was brawny edema of the wall and of the vulva. Blood was cultured immediately; the next morning it had a heavy growth of B. coli. Roentgen studies were made, and the child was operated on for obstruction of the bowel that afternoon. When the abdomen was opened a large gangrenous loop of bowel presented. The area of gangrene was sharply demarcated, and twists of this and other loops of bowel were readily replaced to normal position. The volvulus was not extensive or tightly bound and involved more than the gangrenous section of bowel, and it was felt that the twist may have been secondary rather than primary. The gangrenous part was resected, and an anastomosis was made as quickly as possible. On pathologic examination the resected portion of bowel had numerous perforations. Administration of sulfanilamide, which had been started before operation, was continued with large doses, and the child survived six days postoperatively. The blood cultures continued to yield B. coli, and at autopsy a lumbar puncture revealed turbid yellow fluid which on direct smear, uncentrifuged, was teeming with B. coli. At present there is no positive proof that sepsis preceded the gastrointestinal condition, but the findings are suggestive, and further investigation is indicated. The assumption that sepsis is secondary to perforation may well be faulty.

Even the babies that are born sterile remain so for an exceedingly short time after delivery, and ability to cope independently with bacteria is as essential as the establishment of normal cardiac and respiratory

41. Slemons, J. M.: Placental Bacteremia, J. A. M. A. **65**:1265 (Oct. 9) 1915.

42. Penfold, W. J., and Butler, H. M.: The Infection of the Placenta and the Foetus by Induction of Labour in Eclampsia, M. J. Australia **1**:336, 1933; Placental Infection in Induced Labour with Special Reference to Its Relationship to Foetal and Neonatal Mortality, ibid. **2**:128, 1937.

43. Kobak, A. J.: Fetal Bacteremia: A Contribution to the Mechanism of Intrauterine Infection and the Pathogenesis of Placentitis, Am. J. Obst. & Gynec. **19**:299, 1930.

function. Bacteriologic studies on the meconium after birth (Hall and O'Toole [44]) have shown that the intestinal tract is invaded by B. coli within the first few hours. In a high percentage of cases streptococci are also present. By the third or fourth day the intestinal flora is established. Bonar [45] found that the stools of babies in the newborn nursery often contained occult blood on the third to the sixth day after birth. The intestinal mucosa of a child examined post mortem showed congestion. There are many reports on ulceration in cases of fatal melena of the newborn. In several cases of perforation in this series inflammation of the mucosa of other parts of the intestine was present. Factors that may depress the normal immune mechanism are deep asphyxiation, trauma during delivery, and drugs and anesthetics administered to the mother. An illustrative case was observed at the Hospital for Children in 1938. In delivery of twins the cord was found wrapped tightly around the neck of the first twin; it was cut to facilitate delivery. After birth of this baby it was apparent that the cut cord was that of the second twin. It was nine minutes between the cutting of the cord and the second delivery. Resuscitation was difficult but was accomplished. The infants were boys and apparently identical; the birth weights were over 4 pounds (1,814 Gm.). On the next day the asphyxiated twin was breathing rapidly and his temperature was 104 F. He was placed in an oxygen tent with improvement, but on the fourth day vomiting and diarrhea developed, and on the sixth day the child died. Cultures of heart blood and spinal fluid yielded B. coli. Autopsy revealed fresh vegetations on the heart valves and marked ileitis. The brother thrived normally. Deep asphyxiation was undoubtedly the main factor contributing to sepsis in this case.

If it is granted that the fetus in utero is usually protected against bacteria and that even if bacteria gain entry the majority of fetuses survive the invasion, there is still the possibility that in a rare case (and perforation is rare) infection may play a role. Not all infections of the newborn are fatal. Abscess of the breast occurs in the nursery, and sometimes an infant has cystitis or pyelonephritis. These infections probably are metastatic either via the placenta, just before or at birth, or from the intestinal tract when the flora is established there. Sepsis occurs at other times and may go unrecognized. The newborn infant does not as a rule respond with the classic inflammatory reactions of an older child or an adult. Meningitis or peritonitis may be observed

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44. Hall, I. C., and O'Toole, E.: Bacterial Flora of First Specimens of Meconium Passed by Fifty Newborn Infants, Am. J. Dis. Child. **47**:1279 (June) 1934; Intestinal Flora in Newborn Infants, with a Description of New Pathogenic Anaerobe, ibid. **49**:390 (Feb.) 1935.

45. Bonar, B. E.: Blood in the Stools of the Newborn, Am. J. Dis. Child. **36**:725 (Oct.) 1928.

at autopsy (Dunham [46]) although during life there were no symptoms pointing to it. However, unusual signs, such as slight edema, spots of gangrene or merely diarrhea, should make the attending doctor suspect sepsis. These infants behave more like a culture medium than like a living organism combating infection. They simply turn sour and die.

Finally, the delivered baby may be unable to withstand his first contact with bacteria, and inflammation, localized or general, of the intestinal tract may occur. At other times ulceration with hemorrhage or perforation takes place.

A search of the series for prenatal pathologic conditions is unfortunately unsatisfactory. Careful antepartum and prenatal observation is a relatively new science, and when in records of the early cases pregnancy or birth or both are described as normal the term must be taken as relative. Even the scant information given is worthy of note. Of 83 cases listed in the table, in 20 some abnormality was noted in the maternal history. There were 8 cases of premature birth in the group, and in 3 of these instances there was in addition a pathologic condition in the mother; in 1 case toxemia, in another rheumatic heart disease and nephritis and in a third hydramnios and postpartum fever were noted; 1 mother had placenta praevia. In 2 cases there was cesarean delivery and in 2 difficult labor with deep asphyxiation of the infant. Twice perforation occurred in a twin. It is also interesting that 4 patients were Negro and 2 Chinese. One child had hydrocephalus with other anomalies, and another had harelip and cleft palate.

PROGNOSIS

The prognosis of perforation of the gastrointestinal tract of the newborn is obviously bad. In this series Selinger's [47] patient is the only one that recovered. This infant of 3 months had a walled-off perforated ulcer of the stomach; gastrojejunostomy was performed, and the infant survived. An interesting case of pneumoperitoneum was recorded by Tunger.[48] A twin boy became distended on the fifth day after birth. He had no fever, continued taking his food well and had normal bowel movements. A flat plate of the abdomen showed free air in the peritoneum. The abdomen continued to distend for a few days, but as the child was thriving no treatment was instituted. By the eighteenth day the distention had subsided, and roentgen study repeatedly showed

46. Dunham, E. C.: Septicemia in the Newborn, Am. J. Dis. Child. **45**:229 (Feb.) 1933.

47. Selinger, J.: Peptic Ulcers in Infants Under One Year of Age, Ann. Surg. **96**:204, 1932.

48. Tunger, H.: Spontan Pneumoperitoneum bei einem Neugeborenen, Monatschr. f. Kinderh. **67**:264, 1936.

normal conditions. This is the only recorded case of this type found. It is not listed in the present series because there was no way of knowing where the air came from. Presumably a perforation had occurred high up in the gastrointestinal tract; it was probably a minute opening which sealed over, and the body managed the infection without symptoms. These cases as well as some in which the patient died in spite of treatment will lead the optimist to hope that some patients may be saved in the future.

TREATMENT

In a high percentage of the reported cases diagnosis was made only at autopsy. By the aid of roentgen examination the diagnosis has been more frequently made earlier; however, in not all cases is the condition revealed even by this means. With the low incidence, few physicians will have a chance to benefit by past clinical experience. Gastric lavage or gavage and enemas are contraindicated. Supportive treatment alone is probably of little value after the perforation has occurred. Edema is present, and subcutaneous fluid is therefore usually not given. Blood transfusions, which have been used before and after operation, are logical therapy, not only as aid against the shock but for the possible immunologic value of the adult blood. If bleeding has occurred, as was the case in a fair percentage of the series, blood is particularly indicated. In a case of rupture with perforation peritonitis, the only therapy offering a chance is operative procedure. Without it, there is no knowledge of the size of the tear, and if the peritoneal cavity is full of intestinal contents, the chance of recovery is nil. Sudden perforation, in an infant as in an adult, necessitates immediate surgical intervention. It is well, however, to remember Tunger's case if no adverse symptoms are present.

In 13 of the 83 cases in the present series operation was performed, and in 4 cases the perforation was not found. The operations were divided as follows: Of the 44 patients with peptic ulcer, 7 were operated on and in 1 case the ulcer was not found. One patient recovered after gastrojejunostomy. Of 39 patients with rupture of the bowel, 6 were operated on, and in 3 instances the ulcer was not found. If a perforating ulcer is found it should be sewed up. Walled-off perforations, cysts and other complications have to be treated according to the pathologic condition. Enterostomy should not be performed. All authors are agreed that infants do not tolerate enterostomy or colostomy. If, as the few bacteriologic studies indicate, infection plays a major role. whether primary or secondary, a line of attack supplementary to surgical treatment is indicated. In only a single case of the series was sulfanilamide used, the case reported jointly by Mathes and myself. We had no precedent for this therapy. The immediate results were gratifying but the final outcome fatal. It is our conclusion that the

drug may not have been given in large enough doses or consistently enough. In the case of the Japanese child with resection of the bowel, reported earlier in this paper, however, much larger doses were given without sterilizing the blood stream of the infant. It may be asking far too much of modern medical therapy to expect a newborn infant to survive gangrene of the bowel, resection and sepsis. Less desperate situations may offer hope, and it is possible that combining surgical therapy with administration of sulfanilamide or of a similar drug will save the patients, with a more favorable outlook in the future. The babies observed have withstood surgical procedures in a remarkable fashion.

It is probably more profitable, however, to look to prevention instead of to cure. Adequate nutrition and freedom from infection may be of importance during the prenatal period. At the time of labor factors predisposing to infection are a long dry labor, frequent examinations, instrumentation, narcosis by drugs and deep asphyxiation by anesthesia. The infant's immunity may be adversely affected by drugs, anesthesia of the mother, asphyxiation due to prolonged labor or other accidents of labor such as trauma or chilling. The administration of adult whole blood to the infants born with difficult or abnormal labor may be of more benefit immunologically than hematologically and should be a standard procedure.

CASES NOT INCLUDED IN THE TABLE

Although in the present series I stretched a point to include traditional cases, a number of cases are omitted that have been listed in one or more previous series. These cases deserve some comment, especially as they will interest future searchers in this field. Adler [49] is frequently quoted. His article deals with autopsies of 26 children with ulcer (the ages are not given), in 9 of whom perforation occurred. Sawtell [50] reported on ulceration of the stomach, but there was no record of perforation; the same is true of Homen,[51] though his original article was not obtainable.

Curling [52] has been mentioned in a number of articles with incorrect as well as with correct references, but when the original article was consulted his patients were found to be children with burns who were all well beyond the newborn period.

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49. Adler, H.: Gastric Ulcers in Childhood, Am. J. M. Sc. **133**:135, 1907.

50. Sawtell: Hematemesis and Melaena in Which Blood Was First Vomited Twenty-One and a Half Hours After Birth, M. Times & Gaz. **2**:547, 1885.

51. Homen, E. A.: Beitrag zur Kenntnis der Malaena neonatorum, Finska läk.-sällsk. handl. **32**:347, 1890; abstracted, Jahrb. f. Kinderh. **33**:176, 1891.

52. Curling, T. B.: On the Acute Ulcerations of the Duodenum in Cases of Burns, Med.-Chir. Tr. **25**:260, 1842.

The cases reported by Landau,[53] Kling,[54] Flesch [55] and Spiegelberg [56] were not included in the table because the conditions described do not come under my definition of true perforation. In these cases the ulceration, however, was deep, extending to the serosa. In the cases of Cienchanowski and Glinski,[57] Ludewig,[58] Browicz [59] and Pfaff [32] the condition was secondary to obstruction. In Bloch's [60] case it was associated with pyloric stenosis. In Freund's [61] case it was secondary to gastrojejunostomy for pyloric stenosis. It is not clear whether or not Porter's [62] patient had a perforation.

Keating's case was referred to by Jachens [22] and by Russell [63] without a reference, and the original article could not be found. Kendall's case is in Thiele's [64] table, but the reference was not available.

Except when noted, in all the cases the diagnosis was verified by the author. This review of the literature was made possible through the cooperation of the librarians at the medical libraries of the University of California and Stanford University.

SUMMARY

Spontaneous perforation of the gastrointestinal tract, though rare, may occur in the stomach, duodenum or any portion of the bowel.

Rapid distention of the abdomen is the most consistent finding; the diagnosis frequently can be determined preoperatively by roentgen study. Pneumoperitoneum is not unusual.

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53. Landau, L.: Ueber Melaena der Neugeborenen, nebst Bemerkungen über die Obliteration der foetalen Wege, Breslau, [O. Gustmann], 1874.

54. Kling, L.: Ueber Melaena neonatorum, Inaug. Dissert., Munich, J. Schreiber, 1875.

55. Flesch, H.: Zur Diagnose und Pathogenese des Duodenalgeschwürs in Säuglingsalter, Jahrb. f. Kinderh. **76**:542, 1912.

56. Spiegelberg: Zwei Fälle von Magen-Darmblutung bei Neugeborenen in Folge von Duodenalgeschwüren, Jahrb. f. Kinderh. **2**:333, 1868-1869.

57. Cienchanowski, S., and Glinski, L. K.: Zur Frage der kongenitalen Dünndarmatresie, Virchows Arch. f. path. Anat. **196**:168, 1909. Cienchanowski, S., 1898, cited by Rudnew.[17]

58. Ludewig, A.: Ueber einen Fall von spontaner Darmruptur bei Atresia ani, Inaug. Dissert., Greifswald, C. Sell, 1891.

59. Browicz, cited by Rudnew.[17]

60. Bloch, C. E.: Die angeborene Pylorusstenose und ihre Behandlung, Jahrb. f. Kinderh. **65**:634, 1907.

61. Freund, W.: Ueber Pylorusstenose im Säuglingsalter, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **11**:309, 1908.

62. Porter, J. A.: Peritonitis in the Fetus, Philadelphia M. J. **6**:132, 1900.

63. Russell, T. H.: Spontaneous Rupture of the Intestine of the Newborn, Proc. Connecticut M. Soc., 1927, p. 178.

64. Thiele, P.: Ueber Geschwürsbildungen des Gastroduodenaltractus im Kindesalter, Ergebn. d. inn. Med. u. Kinderh. **16**:302, 1918.

Rupture of the stomach or duodenum has usually been found to be due to perforation of a peptic ulcer. The cause of rupture in the remaining part of the gastrointestinal tract is not as clear.

Perforation above obstruction is not considered in this paper. Other etiologic factors discussed are trauma, congenital defects, injuries and accidents occurring during rotation and particularly infection occurring in utero, during delivery or at the time of establishment of the intestinal flora.

The prognosis is bad. Treatment should be directed toward surgical repair and combating infection.

A table of the reported cases of spontaneous perforation has been compiled. Brief comments are made on another group of cases not included in this table but listed in other series of cases.

News and Comment

GENERAL

Physicians Certified by American Board of Pediatrics.—The following physicians were certified by the American Board of Pediatrics after the examinations in New York on April 25 and 26, 1939:

Eleanor L. Adler, Yonkers, N. Y.; Charles V. Baker, Brooklyn; Harry F. Becker, Battle Creek, Mich.; Sidney Blumenthal, New York; Sydney M. Borowsky, Philadelphia; J. Edmund Bradley, Baltimore; Elizabeth Brakeley, Montclair, N. J.; Henry Cohen, Brooklyn; Irvin J. Cohen, Brooklyn; Harold William Kinghorn Dargeon, New York; Curt Hermann Falkenheim, Rochester, N. Y.; George J. Ginandes, New York; Jerome Glaser, Rochester, N. Y.; Harry H. Gordon, New York; John E. Gundy, Port Chester, N. Y.; Albert Scott Harden Jr., Maplewood, N. J.; Edwin Adams Harper, Lynchburg, Va.; Fred Herbert Harvie, Belleville, Ontario, Canada; David Hauptman, Brooklyn; Robert C. Hood, Washington, D. C.; Frank Jay Jacobson, Providence, R. I.; Edmund N. Joyner III, New York; Herbert Richard Kobes, Augusta, Maine; Irving Kowaloff, Brooklyn; Jacob D. Leebron, Philadelphia; Charles Joseph Leslie, New York; Harold Levy, Brooklyn; Henry H. Lichtenberg, New York; John Alden Lichty Jr., Rochester, N. Y.; Harold Lipschitz, Brooklyn; Joseph P. Michelson, Brooklyn; William Paris, Chelsea, Mass.; Milton Rapoport, Philadelphia; Solomon Rauch, Brooklyn; Rudolf L. Roddy, Philadelphia; Irwin Schiff, Brooklyn; Richard Schorr, New York; Joseph Schwartzman, Brooklyn; D. William Scotti, New York; Lydia Shapiro-Mindlin, New York; Eli Y. Shorr, New York; Louis Spekter, Hartford, Conn.; Martin L. Stein, Brooklyn; Harry Strongin, Brooklyn; Clifton C. Taylor, Bridgeport, Conn.;; Abram S. Tepper, Far Rockaway, N. Y.; William J. Turtle, Boston; Anna E. Wagner, Brooklyn; Virginia Travell Weeks, Brooklyn; Daniel A. Wilcox, Mount Kisco, N. Y.

The following physicians were certified by the American Board of Pediatrics after the examination in St. Louis on May 14, 1939.

Alexander John Alexander, Lexington, Ky.; Ralph Newton Barlow, Logan, Utah; Jack Basman, Charleston, W. Va.; Jack Chesney, Knoxville, Tenn.; Peter G. Danis, St. Louis; Mark W. Dick, Grand Rapids, Mich.; Clayton Thomas Joseph Dodge, East Cleveland, Ohio; Ralph E. Dyson, Minot, N. D.; A. R. Eveloff, Springfield, Ill.; Theodore Herzl Goldman, Los Angeles; C. Jack Harrison, Chicago; Stanley L. Harrison, St. Louis; H. Sidney Heersma, Kalamazoo, Mich.; Frederick A. Jacobs, St. Louis; Joseph Cabell Jaudon, St. Louis; Reuben I. Klein, Chicago; Ralph Hess Kunstadter, Chicago; Matthew M. Lewison, Chicago; J. Keller Mack, Louisville, Ky.; Thomas Myers, St. Paul; George T. O'byrne, Tyler, Texas; Maurice C. O'Hern, Chicago; Henry George Poncher, Chicago; Alwin C. Rambar, Chicago; William H. Reals, Chicago; Roland Boyd Scott, Chicago; Mandel Lawrence Spivek, Chicago.

UNIVERSITY NEWS

University of Chicago.—A fellowship in pediatrics at the University of Chicago has been established by a gift of $25,000 from the Benjamin J. Rosenthal Charities. This will provide $1,000 a year.

New York University.—The department of pediatrics of the New York University has received $5,000 from Mrs. Edith H. de Long.

Abstracts from Current Literature

Metabolism; Infant Feeding; Milk and Other Foods

NUTRITIONAL OEDEMA IN CHILDREN IN EGYPT. H. SHUKRY and M. A. MAHDI, Arch. Dis. Childhood **13**:254 (Sept.) 1938.

Eighteen cases of a gastrointestinal disorder with edema were collected, in 3 of which pulmonary tuberculosis and otitis media were also features. The patients all showed marked hypoproteinemia, a drop in the cholesterol content of the blood and a rise in the chloride content of the edema fluid. This picture is similar to the starvation edema of animal experiments. Prolonged starvation produces profound metabolic changes, associated with marked hypoproteinemia and with retention of chlorides in the tissues. Marked damage of the liver is often noticed post mortem, suggesting that the role of the liver in the metabolism of protein may also be disturbed. KELLY, Milwaukee.

DIET IN HEALTH AND DISEASE: GENERAL PRINCIPLES OF DIET IN CHILDHOOD. B. RIVET, Practitioner **142**:115 (Jan.) 1939.

"Throughout childhood the diet must be composed of the same essential constituents, the amount increasing with the age of the child. The diet must provide sufficient calories, derived mainly from carbohydrate and fat foods, protein for growth and repair of tissues, and mineral salts, vitamins and water to maintain the body in good health. To ensure that all the elements are present, general mixed feeding from an early age is desirable, with the inclusion of a good choice of protein foods, cereals, fruit and vegetables." GELSTON, San Francisco.

MODE OF ACTION OF VEGETABLES IN THE FEEDING OF INFANTS. B. SORIA, Bull. Soc. de pédiat. de Paris **36**:234 (April) 1938.

This is a brief summary of the results of an investigation of the effects of vegetables in the digestive tracts of the infants. Vegetables produce a reduction in the secretion of gastric juice. With different vegetables there is a wide variation in the emptying time of the stomach. Those with high cellulose and high hydrocarbon content leave the stomach sooner. Their water content plays no part in this. Tenderness, trituration, canning, and addition of flour, butter or oil, as well as feeding smaller quantities, lessen the stay of vegetables in the stomach. Prolongation of the emptying time leads to diminution of appetite and increased secretion. There is a variation in the time of transit through the intestinal tract for different vegetables. BENJAMIN, Montreal, Canada.

IS GOAT'S MILK HARMFUL AS INFANT'S FOOD? K. SCHWARTZER, Med. Klin. **34**:937 (July 15) 1938.

A high proportion of infants fed goat's milk present anemia (which may be severe) and poor physical development. Even when fed in combination with breast milk and with supplementary foods goat's milk is harmful. After the first year of life it is apparently not harmful. SIEMSEN, Chicago.

BACTERIAL GROWTH AND LACTIC ACID PRODUCTION IN CITRIC ACID MILK. W. GOETERS, Ztschr. f. Kinderh. **60**:77 (Aug. 26) 1938.

Citric acid milk was found to have a furthering influence on the growth of the most important lactic acid bacteria and an inhibitory influence on the growth

of Bacillus coli, micrococci and tetracocci. No influence on the growth of Proteus vulgaris and Bacillus subtilis was noted. The influence on certain other bacteria was indefinite.

The percentage of lactic acid produced by B. coli is 0.09; that of lactic acid produced by Bacillus aerogenes is 0.3. The latter percentage is supposed to influence the metabolism of the healthy infant favorably. SIEMSEN, Chicago.

CITRIC ACID FERMENTATION BY BACTERIA. W. GOETERS, Ztschr. f. Kinderh. **60**:87 (Aug. 26) 1938.

Investigations made on citric acid milk revealed that Bacillus lactis aerogenes, Proteus vulgaris, Bacillus subtilis and most of the milk and fecal streptococci caused fermentation of citric acid, whereas 12 strains of Bacillus coli did not.

SIEMSEN, Chicago.

CHANGES BROUGHT ABOUT IN THE QUALITATIVE COMPOSITION OF THE BACTERIAL FLORA IN INFANTS' STOOLS BY CITRIC ACID MILK. W. GOETERS, Ztschr. f. Kinderh. **60**:92 (Aug. 26) 1938.

Goeters found that in babies given citric acid milk the ratio colon bacilli: putrefactive bacteria: lactic acid bacteria changes from 1: 1.3: 1.2 to 1: 0.5: 5.1 (average). The reaction of the feces and urine becomes more acid. The stools of babies given citric acid milk simulate the stools of babies fed breast milk.

SIEMSEN, Chicago.

Vitamins; Avitaminoses

RECENT OBSERVATIONS ON THE TREATMENT OF SIX HUNDRED PELLAGRINS, WITH SPECIAL EMPHASIS ON THE USE OF NICOTINIC ACID IN PROPHYLAXIS. T. D. SPIES, J. M. GRANT, R. E. STONE and J. B. MCLESTER, South. M. J. **31**:1231 (Dec.) 1938.

The authors conclude: 1. Nicotinic acid is a vitamin. 2. Pellagra results at least in part from a dietary deficiency of nicotinic acid or of some closely related substances. 3. The lesions due to this deficiency can be prevented or made to heal by administration of nicotinic acid, sodium nicotinate, nicotinic acid amide or the diethyl amide of nicotinic acid, in large daily doses. 4. The peripheral neuritis of pellagra is due to a deficiency of vitamin B_1 and can be relieved by administration of this vitamin, but is not improved by nicotinic acid therapy. 5. The regimen now recommended (a full diet with nicotinic acid and, when necessary, vitamin B_1) represents an advance over anything yet offered in the way of treatment for pellagra. However, as one sees more and more pellagrins, one is forced to conclude that the nicotinic acid supplement to the diet relieves only a deficiency of nicotinic acid or of closely related substances and that its greatest value comes when it is added to a full, well balanced diet.

SCHLUTZ, Chicago.

TREATMENT OF PELLAGRA WITH SPECIAL REFERENCE TO THE USE OF NICOTINIC ACID. J. M. RUFFIN and D. T. SMITH, South. M. J. **32**:40 (Jan.) 1939.

Ruffin and Smith state that nicotinic acid in doses of 1.5 mg. per kilogram (about 100 mg.) per day, given parenterally, is highly effective in treatment for pellagra. The oral dose should be larger (100 mg. two to three times daily). Doses as large as 1 Gm. per day produce definite toxic symptoms in normal persons.

Nicotinic acid does not affect associated deficiencies, particularly that in vitamin B_1.

Intravenous administration of dextrose and of physiologic solution of sodium chloride is extremely important in the treatment of critically ill patients.

In the routine treatment of pellagrins, nicotinic acid should be supplemented by a well balanced diet. SCHLUTZ, Chicago.

INFLUENCE OF VITAMINS C, B_1 AND B_2 ON THE CHOLESTEROL CONTENT OF THE BLOOD IN CHILDREN. B. VASILE and F. PECORELLA, Méd. inf. **9**:330 (Nov.) 1938.

Each series of observations was made on 5 children between 4 and 10 years of age.

1. Ascorbic acid in daily doses of 200 mg. was given hypodermically for eight days; on the ninth day 200 mg. of ascorbic acid was given intravenously. The average cholesterol content of the blood before this injection was 85 mg. per hundred cubic centimeters; one-half hour after the injection it was 69 mg.; two hours after, 101 mg., and eight hours after, 105 mg.

2. Daily doses of 10 mg. of vitamin B_1 (betaxin) were injected hypodermically for eight days; the average cholesterol content of the blood was 102 mg. per hundred cubic centimeters before this treatment started and 76 mg. afterward.

3. Two milligrams of lactoflavine was given daily for eight days. The average cholesterol content of the blood was 93 mg. before and 111 mg. after this treatment.

Each of the 5 children in each series had cholesterol values strictly comparable with the averages reported.

HIGGINS, Boston.

ULTRAVIOLET RAY OF DIFFUSE DAYLIGHT AND ITS THERAPEUTIC UTILIZATION. H. MAI, Ztschr. f. Kinderh. **60**:154 (Aug. 26) 1938.

As a result of the breaking and bending of light waves by atmospheric molecules, diffuse daylight may contain more ultraviolet waves than direct sunlight when the sun is low. Using a cadmium photocell, Mai measured the ultraviolet radiation reaching different parts of a hospital veranda exposed to diffuse daylight but not to direct sunlight. The amount of ultraviolet radiation was found to be proportionate not to light intensity (as measured by a light meter) but to the area of sky visible. On bright days a considerable amount of ultraviolet radiation was recorded. Curves and graphs for various weather conditions and for different times of the year are presented. Ultraviolet ray lamps were studied with the photocell, and the results were compared with those obtained with daylight.

Mai thinks that diffuse daylight has antirachitic value and that prolonged exposure to it may be as beneficial as a short exposure to direct sunlight. A patient with severe rickets observed during March and treated by the open air method made a rapid clinical recovery, and the blood phosphorus rose from a value half that of normal to normal in a short period of time.

SIEMSEN, Chicago.

STUDIES ON LOCAL PRODUCTS OF HUNAN: III. THE VITAMIN C CONTENT OF "VEGETABLE WATER." T. F. SU, Chinese M. J. **54**:351 (Oct.) 1938.

Su reports an experiment with 14 varieties of vegetables obtained from a city market. "Vegetable water" is used in infant feeding, and it was found that the vitamin C content was highest in New Zealand spinach, cabbage and mallow. These are recommended ordinarily, as oranges are too expensive for common use.

NEFF, Kansas City, Mo.

RECTAL ABSORTION OF VITAMIN C. R. KAWAMURA, Acta pædiat. japon. **44**:1031 (July) 1938.

Kawamura had noted previously that clinical improvement followed rectal administration of ascorbic acid in a case of essential thrombopenia and in a case of infantile scurvy. In rabbits administration of vitamin C by a similar method was followed by an 82.8 per cent increase of vitamin C in the aqueous humor of the eye. This peak was reached four hours after the start of administration.

KATO, Chicago.

INVESTIGATIONS OF THE VITAMIN C STANDARD IN HEALTHY CHILDREN AND IN CHILDREN SUFFERING FROM GINGIVITIS. C. W. HERLITZ, Acta pædiat. **23**:43, 1938.

In a social and hygienic survey of nearly 20,000 persons in Sweden from 1929 to 1931, certain paradoxic findings made it apparent that a need existed for more precise information concerning the causes of gingivitis and, in particular, concerning its relation to occult deficiency of vitamin C. To this end Herlitz made a study of the vitamin C saturation of two groups of children, the first with healthy gums, the second presenting gingivitis.

Of the several available physiologic technics, one was chosen which consists in determining the concentration of ascorbic acid in the blood serum before and two hours after oral ingestion of 10 mg. of ascorbic acid per kilogram of body weight. The assumption underlying this technic is that the rise of ascorbic acid in the serum is directly proportional to the degree of saturation of the body at the time of the test. The titrations were made by the author's modification of the methylthionine chloride (methylene blue) method described by Martini and Bonsignore in 1934 and independently by Lund and Lieck in 1936. It consists in reductive decolorization of methylene blue under the influence of intense illumination supplied by a 300 watt lamp.

The study included 44 healthy children and 57 with gingivitis. The ages were between 3 and 16 years. A detailed history of the customary diet was obtained from each patient.

The values for ascorbic acid in the blood serum after "loading" were found to correlate with the subject's alleged consumption of raw fruit much better than the fasting values. With respect to saturation with vitamin C no significant difference was found between the healthy children and those exhibiting gingivitis. In several children in both groups low values were brought to normal in three weeks by adding moderate amounts of fruit to the diet.

The following statistics merit reporting: Average values of serum ascorbic acid of children consuming one orange or one apple daily: fasting, 0.71 ± 0.073 mg. per hundred cubic centimeters; two hours after oral ingestion of 10 mg. of ascorbic acid per kilogram, 1.87 ± 0.111 mg. Children receiving raw fruit not oftener than once a week: fasting, 0.24 ± 0.025 mg.; after two hours, 0.69 ± 0.050 mg. From these data the conclusion is drawn that a fasting value below 0.40 mg. combined with a two hour value below 1 mg. suggests a low intake of vitamin C.

McCUNE, New York.

Hygiene; Growth and Nutrition; Public Health

A CONSIDERATION OF PRESENT DAY NEWBORN NURSERY PRACTICE. M. L. SPIVEK, J. A. M. A. **111**:1065 (Sept. 17) 1938.

To correct the dangers of contagion in nurseries for the newborn, Spivek advises either increased regulation and tightening of nursery technic or dispersion of the infants. As the means of dispersion he suggests individual cubicles completely equipped, three to four bed nurseries closely associated with the mothers' beds, the keeping of the newborn infant in or next to the mother's room, two day hospitalization or delivery at home.

HEERSMA, Kalamazoo, Mich.

PHYSICAL INDICES AND CLINICAL ASSESSMENTS OF THE NUTRITION OF SCHOOL CHILDREN. R. H. JONES, J. Roy. Statist. Soc. **101**:1, 1938.

The problem of discovering undernourished children in England offered Jones an opportunity to analyze statistically the deviation in opinion of what constitutes undernourishment. His objective is the devising of a simple mathematical method by which children needing supplementary food may be determined.

At present a child is examined by the medical officer of the school only three times during his school life, unless he is recommended for special inspection by

teachers or parents. To improve this system, one of two alternatives is suggested: (1) rapid reviews of the group at more frequent intervals and selection of those appearing undernourished for detailed examination, or (2) "screening out" through the use of an index based on physical measurements requiring little technical skill and reexamining those falling below a set minimum.

For this study schools whose children came from various economic planes were selected. The medical officers checked the efficiency of their clinical judgment of the nutritional status of the children by reexamining the same group six months later. There was a mathematically significant failure to agree with themselves, demonstrating the inaccuracy of clinical impressions. In a second phase five physicians checked each other in several instances, and there was but a small percentage of agreement. In more than half the cases the doctors failed to agree on whether a boy was physically subnormal or not.

In this inquiry nutrition was classified as follows: 5, excellent; 4, normal; 3, slightly subnormal; 1 or 2, bad.

Statistical analysis of the medical officers' reports shows that children considered well nourished were larger in their physical measurements and heavier. It was found that the physicians' opinions could be correlated with weight-height and weight-chest ratios.

From this observation it was hoped that an index could be formulated utilizing (1) simple measurements made by school nurses, (2) a table of simple calculations and (3) the existing medical staff.

It was found that the weight-height ratio (Quetelet) and the weight-height ratio × (381 — age in months)/54 (Tuxford) recorded in the metric system most nearly fulfilled all requirements. Dr. Tuxford devised a formula for the English system—(pounds/inches) × (379 — age in months)/0.3—which may be substituted. The "nutrition quotient" for the average child according to the Tuxford index is about 1,000. The index diminishes as nutrition falls. Jones decided to use 970 as the lower limit of normal. This screened out 32 per cent of his group. Eighty per cent of these had been placed in grade 3 and 20 per cent in grade 4 by the examining physicians. None of those in grade 5 (superior) was screened by the index.

He concludes that Tuxford's index may be relied on as confidently to select the undernourished as a medical officer chosen at random. BLATT, Chicago.

RECOMMENDATIONS ISSUED BY THE FOURTEENTH CONGRESS OF HYGIENE. Bull. Soc. de pédiat. de Paris **35**:720 (Dec.) 1937.

To avoid fatigue in primary school children the following recommendations were made: The hours of work should be reduced and one-half hour daily should be set aside for physical training, preferably outdoors and in suitable attire, and one-half day weekly, if possible, for supervised sports. The first gymnastic exercise taught should be proper breathing. The age at which a child passes from the nursery to the primary school should vary according to his mentality and physique and the advice of the physician. No class should last for more than an hour.

A reduction of the hours to be spent in secondary schools was also recommended, as well as the appointment of one-half hour daily for physical training, preferably outdoors and in suitable attire, and one-half day weekly for breathing exercises, sports and supervised play, the curricula to be reduced in keeping with the capacity for work of children according to age as advised by physicians (a total of three to four hours, including homework, for children of 8 to 10 years, and six hours for children of 14 to 15 years may be used as a basis). No class should last for more than one hour, and there should never be more than three such consecutive classes; there should be ten minutes for recreation between classes. Five class hours daily should be an absolute maximum, to be reached only after the second year. Teachers should be discouraged from giving dictated courses and should use concrete methods.

In elementary classes competition should be reduced to a minimum. Each class should have a principal teacher, who might, for example, teach literary subjects. Psychologic methods should be introduced, so that parents of abnormal children may be advised as to their ability and suitable instruction given. Medical examination as well as the application of general hygienic measures in class and at home should be carried out.

For the prevention of tuberculosis in school children the entire personnel of every school should be given an annual examination, including a roentgenologic examination and if necessary a bacteriologic examination. All persons known to have arrested lesions should be examined semiannually. Every child should have an annual tuberculin test, performed by a private physician, by a physician at an outpatient clinic or by the school physician, before the beginning of classes.

As regards infants, all nurses should have a physical and roentgenologic examination before they are given cards entitling them to apply for positions to take care of infants, and the entire personnel of every institution for infants should undergo annual examination. Concerning the supply of milk (1) a record of the temperatures of pasteurization should be required and (2) freedom from pathogenic bacteria and a bacterial count not over 100,000 per cubic centimeter, as determined by an approved method, when the milk reaches its point of distribution for consumption. Other conditions such as hermetic sealing of bottles, marking the date of pasteurization and maintenance of a temperature of about 10 C., should be established as soon as possible. The distribution of milk in schools should be under medical, bacteriologic and veterinary supervision. It is urged that laboratories be set up for systematic research concerning the physical, psychologic and social welfare of persons working in the various industries and that a central, eventually international, bureau be established for the integration and dissemination of the results of the investigations.

BENJAMIN, Montreal, Canada.

Prematurity and Congenital Deformities

OXYCEPHALY: A NEW OPERATION AND ITS RESULTS (A PRELIMINARY REPORT). J. E. J. KING, Arch. Neurol. & Psychiat. **40**:1205 (Dec.) 1938.

King describes a new operation for oxycephaly. It consists in making a mosaic of the bones of the cranial vault; i. e., dividing them into ten or eleven segments. The operation was done on a child and was followed by marked improvement.

BEVERLY, Chicago.

SOME BODY MEASUREMENTS OF TEXAS SCHOOL CHILDREN. J. WHITACRE, Bulletin 567, Texas Agricultural Experiment Station, January 1939.

It is generally agreed that the status of bodily growth and nutrition of children may be judged in part by the degree to which recognized standards of body size and proportions are met. But standards are not yet finally determined even for white children, about whom there is more information than about the children of other races. This study with Mexican, white and Negro school children in San Antonio, Texas, shows among them striking similarities in certain aspects of average size and rates of growth and characteristic differences in other aspects. The differences observed emphasize the need of separate racial standards, and this study contributes data that may be used in developing such standards.

Over 7,300 measurements of weight, standing height and sitting height and approximately 3,000 measurements of shoulder width and hip width were made on 928 white, 790 Mexican and 725 Negro school children.

Characteristic Racial Differences.—While the white and Mexican children were very similar to each other in their rates of growth in each of the five measurements, these two races were exceeded in every rate by the Negro except in hip width of boys, which was the same in all three races.

Weight gains were larger between 10 and 14 years than at other ages in all races but more conspicuously in Mexican and Negro than in white children.

There were more marked differences as regards average measurements between Negro boys and girls than between white boys and girls or Mexican boys and girls.

Negro children were shorter in standing height and lighter in weight than white children from 7 to 9 or 10 years old, but above 10 years the Negroes were the taller and heavier. In sitting height, however, Negroes were the shorter at all ages. Negroes were broader of shoulder and narrower of hip than white children.

Mexican children were shorter than white children of the same age in both standing height and sitting height; Mexicans were lighter in weight and slightly narrower through the shoulders and hips.

Mexican children compared with Negroes of the same age were lighter in weight, shorter in standing height and narrower in shoulder width but similar in both sitting height and hip width.

Striking Similarities.—For all races the rate of growth was much the fastest in weight, followed in order by the rates of growth in hip width, standing height, shoulder width and sitting height.

The variation in weight was approximately two to three times as great as the variation in width of shoulders and of hips and approximately three to four times as great as the variation in standing height and sitting height.

In all races girls under 10 or 11 years weighed less and were shorter in both standing height and sitting height than boys of the same age; from 10 or 11 until 14 or 15 years girls exceeded boys in these measurements, but thereafter girls were again smaller than boys. Shoulder widths were similar for boys and girls of the same age in each race; but when not the same the boys exceeded the girls except among 12 and 13 year old Negroes. Girls above 8 or 9 years were wider through the hips than boys of the same race; these differences were more pronounced after 11 or 12 years of age.

Girls of each race varied more among themselves in each measurement than did the boys.

Obviously growth standards for white children should not be used for Mexican or Negro children. FROM THE AUTHOR'S SUMMARY.

SCHOOL HEALTH PROGRAM AND THE PHYSICIAN. B. S. VEEDER, Wisconsin M. J. **38**:17 (Jan.) 1939.

The health program instituted in the schools of the United States in 1894 is an example of accepted socialized medicine. Protection of the child so that school life does not react disadvantageously on his health is important, but provision of medical care for him is not a function of the school. The national health program outlined for schools in 1924 was too idealistic and included many fallacies. In 1934 the American Child Health Association demonstrated the need for changes. It has since become more obvious that the proper, i. e., the most comprehensive examination of the school child can be made best by his regular physician, who knows his background better than it can possibly be known by a hurried school physician. Increasingly the private physician is making such examinations and making the corrections necessary, returning the health card to the school for its records.

Immunization of the child should not be a function of the school. It is the duty, privilege and responsibility of the physician to see that immunization against diseases is done long before school age. Tests of vision and the use of the audiometer with necessary recommendations for further care are perhaps best left to the school. Greater effort at cooperation on the part of both the physician and the school will do much to solve the problem of giving medical supervision to the school child. JANNEY, Wauwatosa, Wis.

TRUE OXYCEPHALY. J. HOWKINS, D. JEFFERISS and R. S. HANDLEY, Lancet **2**:1226 (Nov. 26) 1938.

True oxycephaly must be differentiated from acquired oxycephaly and hypertelorism. In acquired oxycephaly the changes are not present at birth, appearing only in early childhood.

The authors describe oxycephaly in a stillborn infant.

"Some embryonic disturbance affecting skeletal development and operative during the period between formation of the digits and completion of the joints" is as far as they commit themselves as to the cause of this condition.

LANGMANN, New York.

CONGENITAL DISEASE. J. B. S. HALDANE, Lancet **2**:1449 (Dec. 24) 1938.

This scholarly discussion of autosomal dominant and recessive genes and sex-linked, partially sex-linked and irregular inheritance does not lend itself to abstracting.

LANGMANN, New York.

OXYCEPHALY AND ALTERATIONS OF THE OPTIC NERVE. G. P. SOURDILLE and M. DAVID, Bull. Soc. d'opht. de Paris **50**:206 (May) 1938.

A boy of 7 years had had poor vision for one and one-half years, and for the past six months his sight had been diminishing rapidly. At the age of 3 months the child had severe enteritis with abnormally late closure of the fontanels. His head was of the typical tower skull variety. Normal intelligence with emotional instability were noted. The visual acuity of the right eye was 2/10 and that of the left eye 1/12, with correction by a horizontal convex cylinder to 3.5/10 and 1/10, respectively. There was concentric contraction of the visual fields, more marked on the left, to about 40 degrees. The right disk was completely pale, and the left showed pallor only in the temporal region. Roentgenograms of the skull showed the two characteristics of oxycephaly, namely, digital markings of the convexity, here most formidable, and enlargement of the middle fossa. It is the author's belief that in this case the atrophy was due to intracranial hypertension. Decompression resulted in vision of 4/10 for the right eye, while the left remained at 1/10 after six weeks. The question of operation in these cases is open for discussion.

MAYER, Chicago. [ARCH. OPHTH.]

TREATMENT OF A GRAVE CONDITION IN A PREMATURE INFANT WITH ESTROGEN. P. MAYNADIER, Bull. Soc. de pédiat. de Paris **36**:219 (April) 1938.

A premature infant who was not doing well recovered on administration of 4 drops of an estrogen in a teaspoonful of water twice daily.

BENJAMIN, Montreal, Canada.

ORGANIZATION AND FUNCTIONING OF INFANT CONSULTATION STATIONS IN A RURAL AREA. I. NEMOIANU, Méd. inf. **1**:38 (Jan.) 1939.

The principle of the organization of dispensaries for small children in the rural area is based on the regulation established by the minister of health as well as the law of assistance for the mother and child (edict of the department). This principle preconceives the organization of a local committee in every dispensary of a rural area. The commitee is formed from persons who are most interested in the problem of the protection of the child and the mother. These persons do not represent only an interest purely medical and hygienic. The author details the manner of organizing and conducting these dispensaries.

FROM THE AUTHOR'S SUMMARY.

CONGENITAL HEMIHYPERTROPHY OF THE TONGUE. F. LANDSTEINER, Ztschr. f. d. ges. Neurol. u. Psychiat. **162**:605 (May) 1938.

Landsteiner reports the case of a woman aged 37 who had had enlargement of the right side of the tongue ever since she could remember. For three years she had been especially aware of this enlargement and was annoyed by a pulling sensation with an occasional cramplike reaction in the tongue. There was no other evidence of asymmetry. Neurologic and serologic examinations gave normal results. The electrical reactions of the tongue were equal and normal on the two sides. The condition can be considered partially congenital hemihypertrophy.

SAVITSKY, New York. [ARCH. NEUROL. & PSYCHIAT.]

NEEDED ANALYSES OF CHILD WELFARE ACTIVITIES. S. PAPUZINSKI, Zycie Mlodych **7**:127 (May) 1938.

Analyzing the activities in behalf of child welfare in Poland, Papuzinski brings out the point that the institutions caring for children lost in reputation, and the care of these children by private families became popular. The reasons for this were that after the war Poland was poor, there were too many children who needed care, and care in an institution for children was too expensive. Furthermore, Poland was not prepared for that type of work and did not have a properly trained personnel. Even after many years of attention to child welfare in Poland there could be much improvement along these lines. KRUPINSKI, Chicago.

Newborn

CYANOSIS IN THE NEWBORN. A. H. PARMELEE, Illinois M. J. **74**:516 (Dec.) 1938.

In this article Parmelee discusses the various causes and the treatment of cyanosis of the newborn. The several etiologic factors are classified under the respiratory system, the circulatory system and the nervous system.

BARBOUR, Peoria, Ill.

CONGENITAL HAEMOLYTIC ANAEMIA WITH NORMAL FRAGILITY OF THE RED BLOOD CELLS. E. SCHIFF, Arch. Dis. Childhood **13**:264 (Sept.) 1938.

The history of a girl 1 year and 8 months old is reported, in whom in the first days of her life severe hypochromic anemia was present together with enlargement of the liver and spleen. Further examination disclosed all the typical symptoms of congenital hemolytic anemia; the fragility test of the erythrocytes, however, gave normal results in the period of observation. During periodically occurring rises in temperature, no essential changes in the blood could be demonstrated, nor any acceleration of the sedimentation rate. These febrile attacks are considered as equivalents of hemolytic crises. The disease could not be proved to be inherited.

KELLY, Milwaukee.

PNEUMOCOCCIC MENINGITIS OF THE NEWBORN. I. TOMA and V. PETRESCU-COMAN, Méd. inf. **1**:33 (Jan.) 1939.

The authors describe a case of pneumococcic meningitis following an acute rhinopharyngitis in a little girl, aged 10 days. This child died three days after the beginning of the infection. She received as treatment only antipneumococcic serum.

FROM THE AUTHOR'S SUMMARY.

IMPORTANCE OF HEART BLOCK IN THE NEWBORN. D. HEUBNER, Ztschr. f. Kreislaufforsch. **30**:600 (Aug.) 1938.

During delivery of an infant in a hospital it was noted that the rate of the fetal heart sounds was extremely slow, not rising over 80 per minute even after the

fetal head had entered the true pelvis. A healthy baby was born spontaneously; the heart rate also was very slow, but no pathologic phenomena were noted on auscultation. The electrocardiogram showed bradycardia (60 beats per minute). However, the auricular waves were not directly related to the ventricular complex; the T waves were diphasic in leads 2 and 3. In all probability, there was a 2 to 1 block during and after birth.

The electrocardiogram was taken again when the baby was 11 months old and checked once more at 18 months of age. There was a slight systolic murmur at the apex but no other sign of circulatory disorder, and the roentgen findings were practically normal.

In other cases of congenital heart block reported thus far, the patient usually died a short time after birth, and the autopsy showed severe defects. In this case there probably was a mild disorder which cleared up during the early months of the baby's development. ARON, Chicago.

FAMILIAL ICTERUS GRAVIS OF THE NEWBORN. M. PÉHU, R. NOËL and A. BROCHIER, Bull. Soc. de pédiat. de Paris **35**:606 (Nov.) 1937.

Familial icterus gravis neonatorum is commoner than has been recognized. The authors have encountered 5 cases in the past four years. Syphilis plays no part in the pathogenesis. The condition may occur without increased numbers of erythroblasts appearing in the peripheral blood. The bone marrow must be examined for confirmatory evidence. Mothers who give birth to infants with this condition commonly suffer from abortions, miscarriages and stillbirths. Prophylactically, liver therapy is advocated for the mother during pregnancy and blood transfusion for the newborn infant. BENJAMIN, Montreal, Canada.

A CASE OF SUBCUTANEOUS FAT NECROSIS OF THE NEWBORN. J. H. BROERS, Acta dermat.-venereol. **19**:404 (Aug.) 1938.

Typical subcutaneous fat necrosis of the newborn with spontaneous recovery in three months is described. The differential diagnosis is discussed, and the fact that a definite diagnosis can be established histologically only is stressed. Needle-like crystals (palmitin or palmitin-stearin) were observed histologically.

ASTRACHAN, New York. [ARCH. DERMAT. & SYPH.]

Acute Contagious Diseases

A SUGGESTION FOR THE EARLIER RECOGNITION OF KOPLIK'S SPOTS. J. L. STEIN, Arch. Pediat. **55**:722 (Nov.) 1938.

With the aid of the magnifying lens of the electric otoscope, Stein has been able to detect Koplik's spots twenty-four to forty-eight hours in advance of the usual time of their appearance. ORR, Buffalo.

SULFANILAMIDE IN THE TREATMENT OF ONE HUNDRED AND SIX PATIENTS WITH MENINGOCOCCIC INFECTIONS. J. M. WAGHELSTEIN, J. A. M. A. **111**:2172 (Dec. 10) 1938.

Comparing the results of treating patients for meningococcic meningitis with serum, with sulfanilimide and with both, Waghelstein finds in patients adequately treated with sulfanilamide a reduction in mortality from 27 to 12 per cent. The doses used were similar to the recognized amounts, i. e., 1 Gm. per 20 pounds (per 9 Kg.) per day for one week. Four hour oral or nasal drip administration was preferred to subcutaneous or intrathecal injection.

The care of the patient is simplified. Generally two lumbar punctures are all that are required, and in the series reported the cultures were usually negative after one day. Complications from treatment with sulfanilimide were few. Complications from meningitis were unchanged, but recurrences were fewer.

HEERSMA, Kalamazoo, Mich.

TREATMENT OF PREERUPTIVE MEASLES WITH CONVALESCENT SERUM. J. L. KOHN, I. F. KLEIN and H. SCHWARZ, J. A. M. A. **111**:2361 (Dec. 24) 1938.

In order to modify the course of measles it was found necessary to inject intravenously 40 to 50 cc. of convalescent measles serum in the preeruptive stage. This gave positive results in 19 of 20 children. Normal adult serum given in the same stage was not effective in even much larger doses. The convalescent serum must be given at least one day previous to the eruption. Repeated injections seemed to delay the eruption. No reactions to the serum occurred. Conditions in which prevention or abortion of an attack of measles is indicated are mentioned, and the histories of typical cases are included, with descriptions of the abortive course.

HEERSMA, Kalamazoo, Mich.

WHOOPING COUGH: NEW PHASES OF THE WORK ON IMMUNIZATION AND PROPHYLAXIS. L. W. SAUER, J. A. M. A. **112**:305 (Jan. 28) 1939.

Reviewing the results of work up to the present, Sauer reaffirms that Haemophilus pertussis is the etiologic agent of whooping cough. He presents evidence against the possibility that a virus is the cause. Various workers have found atypical strains and Sauer emphasizes the importance of a confirmation of the diagnosis by a history of contact, a definite whoop or paroxysm, typical lymphocytosis, a positive cough plate or a positive complement fixation test. He mentions the conditions to be differentiated.

He introduces a double strength vaccine. The results of immunization are tested by means of complement fixation tests and agglutination tests and by noting the clinical results after exposure.

After the disease has developed, early administration of convalescent serum or of lyophil serum is valuable.

HEERSMA, Kalamazoo, Mich.

EXPERIMENTAL TRANSFORMATION OF VARIOLA TO VACCINIA. E. S. HORGAN, J. Hyg. **38**:702 (Nov.) 1938.

During the past seventy years extensive attempts to transform variola to vaccinia have not closed the question as to whether or not such mutation is possible. Outstanding recent works are here reviewed briefly; for older work Copeman's summary (1898) is referred to. Differences in type of experimental animal and in technic are believed to account for the varying conclusions. Man and the monkey, steer, rabbit, cat, dog, pig, guinea pig, buffalo, donkey, sheep and fowl have been used in these attempted transfers. Horgan presents experimental work to prove that such transition is possible. The variolar material was collected during an outbreak of virulent smallpox, and various animals were used. The method of intratesticular passage, the rabbit being used as a test animal, was successful. Attempts to bring about mutation of the material by the use of intradermal methods of transfer were unsuccessful.

JANNEY, Wauwatosa, Wis.

SUMMARY OF CURRENT PREVALENCE OF COMMUNICABLE DISEASES. Pub. Health Rep. **53**:2217 (Dec. 23) 1938.

In the period from Nov. 6 to Dec. 3, 1938, the incidence of influenza was 30 per cent and that of smallpox 20 per cent above the figures for the corresponding period of the past five years. The figures for the other contagious diseases were below those usual for the season. The average death rate was 11 per thousand.

SANFORD, Chicago.

SUMMARY OF CURRENT PREVALENCE OF COMMUNICABLE DISEASES. Pub. Health Rep. **54**:59 (Jan. 20) 1939.

For the period of Dec. 4 to 31, 1938, influenza and smallpox were above while all of the other contagious diseases were below the usual seasonal levels. The average mortality rate was 11.9 per thousand, which is the lowest since 1931.

SANFORD, Chicago.

PROPHYLACTIC USE OF PERTUSSIS VACCINE (SAUER). C. HOWELL, South. M. J. **31**:1166 (Nov.) 1938.

Howell states that 278 children who were seen before they contracted pertussis and for whom the Sauer type of pertussis vaccine was recommended were followed in private practice for a period varying from six months to four years. During that time 148 children received the full 8 cc. course of Sauer's vaccine, and 130 children received none.

To date, 6.1 per cent of the vaccinated children have contracted whooping cough (usually in a mild form), and 24.5 per cent of the unvaccinated ones have contracted the disease during the same period of time.

Furthermore, only 2 per cent of the vaccinated children contracted the disease later than four months after the vaccination was completed, the period Dr. Sauer believes necessary to establish maximum immunity. SCHLUTZ, Chicago.

TREATMENT OF DIPHTHERIA AND SCARLET FEVER BY ACTIVE IMMUNIZATION. K. SEDLÁČEK, Brit. J. Child. Dis. **35**:175 (July-Sept.) 1938.

This Czechoslovakian author reports that 352 patients with diphtheria were treated successfully by means of toxin neutralized with antitoxin and, in addition, staphylococcus-streptococcus vaccine. Also, 295 patients with scarlet fever were treated successfully—169 with a polyvalent vaccine and milk and 126 with a staphylococcus-streptococcus vaccine with Dick toxin added.

Sedláček states that "in infections accompanied by a rash, the more pronounced the rash, the more favorable the prognosis."

[As in many other parts of the world, diphtheria still seems to be common in Czechoslovakia because of failure to make use of prophylactic immunizations. No reference is made to the vast literature on this subject.—ABSTRACTOR.]

LANGMANN, New York.

THE CAUSATION OF PARALYSIS IN DIPHTHERIA. I. TAYLOR, Brit. J. Child. Dis. **35**:250 (Oct.-Dec.) 1938.

An attempt is made to reconcile opposing views in reference to the underlying causes of diphtheritic paralysis. There are those who regard all forms of paralysis in diphtheria as due to hematogenous toxemia and others who feel that the toxin first attacks the nerves in the locality of the site of the infection and that all other paralyses are produced by diffusion of toxin in the nervous system from the point of entry.

Numerous references are cited. Taylor concludes that there are good grounds for believing that hematogenous toxemia is capable of producing, in addition to generalized paralysis, a type of paralysis similar to the local paralysis found in faucial diphtheria. On the other hand, the close anatomic relation between the local paralysis and the site of infection can leave no doubt that the nervous system is primarily attacked through local absorption of toxin.

LANGMANN, New York.

SULPHANILAMIDE THERAPY IN MENINGOCOCCAL MENINGITIS: REPORT ON THREE CASES. T. C. MORTON, V. S. EWING and J. D. EBSWORTH, Brit. M. J. **1**:1362 (June 25) 1938.

This is a report of 3 cases of meningococcic meningitis treated with prontosil soluble (disodium 4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3′,6′-disulfonate; now known as neoprontosil) intravenously, prontosil album (sulfanilamide) by mouth and antimeningococcus serum intrathecally. All three of the patients recovered. ROYSTER, University, Va.

USE OF PLACENTAL EXTRACT IN AN EPIDEMIC OF MEASLES. T. N. PARISH, Brit. M. J. **2**:65 (July 9) 1938.

In an epidemic of measles in a girls' school placental extract was used as a prophylactic. The author's conclusions may be summed up as follows: Placental extract was used in an endeavor to reduce the severity of the attacks and the number and severity of the subsequent complications. There were no serious reactions following the injections. The extract did not have the effect of preventing or postponing attacks: it rendered the attacks milder, the duration of elevations of temperature shorter and subsequent complications fewer and less severe. It is probable that the immunity conferred by such prophylaxis diminishes fairly rapidly after three weeks.

ROYSTER, University, Va.

MEASLES: THE CONDUCT OF A SCHOOL EPIDEMIC. F. G. HOBSON, Brit. M. J. **2**:171 (July 23) 1938.

The principles for the control of an epidemic of measles in a self-contained school community are discussed, and their application in practice is illustrated in four epidemics. These principles are: 1. Healthy susceptible persons should be permitted to experience a normal attack of measles after exposure to infection. 2. "Delicate" susceptible persons should be protected. Such subjects fall into two categories: (1) those for whom complete protection should be secured; (2) those for whom attenuation of infection should be a sufficient safeguard from undue risks. 3. Environmental hygiene must be strictly practiced in sickrooms in all cases.

Experiences in the use of protective serum are described, and emphasis is laid on the difficulties inherent in dosage. In practice the date of administration should be calculated from the rash of the patient who was the source of the infection. For *protection* a maximum dose should be given at the earliest opportunity after exposure and never later than the third day. For *attenuation* a maximum dose should be given on the sixth day.

ROYSTER, University, Va.

TREATMENT OF MENINGOCOCCAL MENINGITIS WITH M. & B. 693. F. G. HOBSON and D. H. G. MACQUAIDE, Lancet **2**:1213 (Nov. 26) 1938.

Six patients with meningococcic meningitis were successfully treated with sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine; the preparation used was M. & B. 693). A child aged 8 months had a relapse on the forty-eighth day, and a further short course of treatment was necessary to clear up the infection.

It was found that the passage of the drug from the gastrointestinal tract into the blood stream and thence into the cerebrospinal fluid is rapid. The concentration of the drug in the cerebrospinal fluid was found to be approximately half of that in the blood stream.

In 2 cases a concentration of no more than 3 mg. per hundred cubic centimeters in the cerebrospinal fluid produced effective bacteriostasis.

LANGMANN, New York.

RESPIRATORY PARALYSIS DUE TO DIPHTHERIA SUCCESSFULLY TREATED BY MEANS OF THE RESPIRATOR. D. G. HAMILTON, M. J. Australia **2**:1037 (Dec. 17) 1938.

Three cases of postdiphtheritic respiratory paralysis in which treatment in the respirator was successful are described and discussed. In all cases the muscles paralyzed included the diaphragmatic and pharyngeal muscles. One case is recorded in which the intercostal muscles appeared to be slightly affected. Two cases are noted in which palatal paralysis occurred seven days after the onset of the disease. In all cases a long period intervened between the onset of disease and the onset of respiratory paralysis—forty-six, thirty-six and twenty-eight days, respectively. In all cases the patient made little progress for a relatively short period—eleven,

eight and twelve days, respectively. Then in each case a remarkably rapid improvement commenced and was maintained till the respirator was no longer needed. Respiratory and pharyngeal function returned simultaneously.

GONCE, Madison, Wis.

CAPILLARY BRONCHITIS OF DIPHTHERITIC ORIGIN. J. M. PAEZ DE LA TORRE, Arch. de méd. d. enf. **41**:802 (Dec.) 1938.

A boy of 3 months was brought to the hospital on account of obstinate cough. Examination revealed moderate cyanosis and moist rales throughout both lungs. The pharynx was filled with a viscous secretion, and removal of this showed bleeding mucosa underneath. A culture of material from the throat was positive for Löffler's bacillus. Antidiphtheritic serum with inhalations of oxygen and subcutaneous injections of ether and camphor were employed, and the infant was discharged, recovered, in ten days. A sequel in the form of diphtheritic otitis was reported later, and this also yielded promptly to suitable treatment.

AMESSE, Denver.

INFLUENCE OF DIPHTHERIA ON MEASUREMENTS OF THE HEART AND ALTERATIONS OF THE HEART MUSCLE TISSUE. W. MASSHOFF, Arch. f. Kreislaufforsch. **3**:142 (Nov.) 1938.

Linear measurements were taken by the method of Kirch from the hearts of 20 children 1¼ to 16 years of age. These children had succumbed either directly to diphtheria infection or to complications following this infection. Every heart was dilated in some part. On the right side the way of inflow was always more dilated than the way of outflow, while on the left side there was proportional dilatation. This proves that the heart failure was a failure of the right side of the heart and that the dilatation was of myogenic origin (*Hypinogen* and *Hypotonogen,* according to Hering).

In all cases the observer noted cloudy swelling, and fatty and vacuolating degeneration, followed for the most part by reactive infiltration in the interstitial spaces.

ARON, Chicago.

METABOLISM IN EXPERIMENTAL DIPHTHERIA OF THE DOG. P. BAMBERGER and H. E. NEVER, Ztschr. f. d. ges. exper. Med. **104**:511 (Nov.) 1938.

The alterations produced by intoxication of the dog by diphtheria toxin are almost equal to those observed with insufficiency of adrenal cortex: a negative chlorine and nitrogen balance, hypochloremia, increase of nonprotein nitrogen, of urea, of phosphate fractions, of lactic acid, of red blood cells and of hemoglobin and decrease of carbon dioxide and calcium. No changes such as are characteristic for Addison's disease were found in the sodium, potassium and protein contents of the serum.

After introduction of the toxin into the body there are excessive destruction of protein, losses in chlorine and disturbances of the metabolism of phosphate and especially of that of water; carbohydrate metabolism is affected secondarily, causing decrease in the carbon dioxide of the blood and increase in lactic acid (acidosis). Much stress is laid on the decrease in the volume of blood plasma. The pallor and the fall in blood pressure and in the temperature of the skin, so ominous in clinical cases, are explained on this basis.

ARON, Chicago.

ANTERIOR POLIOMYELITIS IN CHINA. A. V. SCOTT, Chinese M. J. **54**:442 (Nov.) 1938.

There is no record of an epidemic of poliomyelitis in China. Seldom has the disease been found in the acute stage. In 25,000 admissions to the hospital of the Peiping Union Medical College, there has been only 1 for a condition diagnosed as acute anterior poliomyelitis.

Chinese records show that the disease has been reported from 14 provinces. Between May 1931 and September 1937 23 children with acute or chronic manifestations were seen in the Cheeloo Hospital Pediatric Clinic. Apparently all of these cases appeared sporadically. NEFF, Kansas City, Mo.

EFFECT OF SUPERSONIC WAVES ON THE VIRUS OF POLIOMYELITIS. M. TATSUMI, S. OGATA, H. KANBAYASHI and K. YOSHIDA, Acta pædiat. japon. **44**:1194 (Aug.) 1938.

Exposing the virus obtained from patients with acute poliomyelitis to supersonic waves for five minutes completely destroyed the toxicity, as proved by inoculation experiments. The authors believe that this effect results from the oxidation attendant on the physical influence of the waves. KATO, Chicago.

RETICULOCYTES IN MEASLES. M. NAGAHAMA, Acta pædiat. japon **44**:1291 (Aug.) 1938.

In measles the reticulocytes are increased, and when complications occur the percentage becomes still higher as compared with the percentage for uncomplicated measles. KATO, Chicago.

GERMAN MEASLES AS A VIRUS DISEASE. Y. HIRO and S. TASAKA, Acta pædiat. japon. **44**:1316 (Aug.) 1938.

Hiro and Tasako prepared a filtrate from the pharyngeal secretions obtained from patients with German measles in the eruptive stage. One cubic centimeter of the filtrate was injected subcutaneously into each of 6 children who had no history of the disease. A filtrate which had been passed through Berkefeld filter W produced typical symptoms of the disease with eruptions in 2 children; in 2 other children the symptoms of the disease appeared but no eruption; and in the remaining 2 children no definite signs of the disease developed. When the filtrate prepared by being passed through a Seitz filter was injected, the disease developed in only 2 of 10 children; in 3 the incubation period was seven days, and in the other 3 it was eight, eleven and seventeen days, respectively. These observations indicate that the virus obtained by filtration through Berkefeld W and Seitz filters is the etiologic agent of German measles. KATO, Chicago.

APPEARANCE OF RETICULOCYTES IN SCARLET FEVER. M. NAGAHAMA, Acta pædiat. japon. **44**:1355 (Sept.) 1938.

In 50 cases of scarlet fever studied by Nagahama the reticulocyte percentage was increased during the eruptive stage and gradually decreased to the normal level with recovery. The percentage was high also during the stage of desquamation, being higher with severe than with slight peeling. KATO, Chicago.

Acute Infectious Diseases

TWO YEARS' OBSERVATION ON THE USE OF ATABRINE AS A PROPHYLACTIC AGENT IN MALARIA. R. A. HILL and M. H. GOODWIN JR., Am. J. Trop. Med. **18**:339 (July) 1938.

Hill and Goodwin studied 1,646 persons on a large plantation where measures for the control of mosquitoes were objectionable or impossible and malaria was prevalent. The initial blood smears indicated a blood parasite index of 16.9 per cent. This was reduced to 0.3 per cent over a period of two years.

The most successful prophylactic agent was atabrine, although quinine seemed to exert a helpful influence in reducing the incidence of malaria. It was difficult to obtain the cooperation of patients taking quinine, and in some cases the recom-

mendation of this drug had to be discontinued because of toxic reactions or idiosyncrasies. No toxic reactions to atabrine were noted. After administration of both atabrine and plasmochin, the number of malaria carriers and of persons exhibiting both gametocytes and schizonts was materially reduced.

BURPEE, Augusta, Ga.

DEMONSTRATION OF SPOROZOITES IN HUMAN TISSUES. M. F. BOYD and S. F. KITCHENS, Am. J. Trop. Med. **19**:27 (Jan.) 1939.

Boyd and Kitchens excised the skin and subcutaneous tissue at the sites where infected mosquitoes were applied. The tissue was removed under aseptic care as soon as possible after removal of the mosquitoes. They were able to demonstrate the sporozoites in the subcutaneous tissues in 1 case.

They also removed lymph glands in the vicinity of the bites and in a single instance found sporozoites in the lymph gland. The removal of the tissue at the sites of inoculation had no effect on the course of the infection. The authors did not think that the finding of the sporozoites in the lymph gland suggested that the lymph passages were the routes by which the main portion of the inoculum reached its destination.

BURPEE, Augusta, Ga.

AN EIGHTH YEAR'S OBSERVATION ON MALARIA IN PANAMA. H. C. CLARK and W. H. W. KOMP, Am. J. Trop. Med. **19**:33 (Jan.) 1939.

Clark and Komp review the results of their work during the eighth year of their study of malaria in Panama. They studied groups of patients treated with atabrine and plasmochin and with quinine and plasmochin. The results as shown in percentages of infection did not favor either combination. They could find no correlation between the rainfall and the parasite rate. The parasite rate during this year was the lowest so far recorded and was believed to be due to the normal decline in rates and to treatment of all persons with parasites in their blood.

The incidence of the various species of parasites in these persons was nearly the same as in previous years, with plasmodium falciparum quotidianum constituting nearly 75 per cent. The authors state that under their plan of control they have been successful in reducing to the vanishing point clinical illness from malaria but not in completely eradicating the disease.

BURPEE, Augusta, Ga.

GONOCOCCAL PERITONITIS. H. BLOCH, B. L. PACELLA and B. LOCASTRO, Arch. Pediat. **55**:714 (Nov.) 1938.

Gonococcic peritonitis is reported as complicating vulvovaginitis in a 4½ year old girl. Smears from the peritoneal fluid taken at the time of operation were positive for the gonococcus. The postoperative treatment consisted in oral and parenteral administration of sulfanilamide. No attempt was made to evaluate the usefulness of the drug in dealing with this disease.

ORR, Buffalo.

RHEUMATIC INFECTIONS IN CHILDHOOD: THE EFFECT OF SURGICAL OPERATIONS ON BLOOD SEDIMENTATION RATE. H. L. BACAL and R. R. STRUTHERS, Canad. M. A. J. **40**:140 (Feb.) 1939.

One hundred children suffering from various manifestations of rheumatic fever were compared with 50 nonrheumatic children as to the morbid effects of operative procedures. The rheumatic children showed more marked alterations in sedimentation rates and greater losses of weight, as well as a greater number of complications, after operations.

MOORE, Omaha.

INCIDENCE OF RHEUMATIC INFECTIONS IN CHILDREN OF OREGON. J. B. BILDERBACK and R. M. OVERSTREET, Northwest Med. **37**:390 (Dec.) 1938.

Patients suffering from rheumatic fever and chorea constituted 3.46 per cent of the medical admissions to the Doernbecher Hosptial (for children), Portland,

Ore., from January 1933 to June 1938, inclusive. Of the 116 patients studied, adenotonsillectomy had been performed prior to the first attack in 39. Rheumatic nodules were seen only twice. The known mortality rate in the group was 9.6 per cent.

ROBERTSON, Omaha.

AMINOPYRINE TREATMENT OF RHEUMATIC ENDOCARDITIS ASSOCIATED WITH ACTIVE RHEUMATIC INFECTION. B. R. HENINGER and G. MCHARDY, South. M. J. **31**:1056 (Oct.) 1938.

Heninger and McHardy state that the results of aminopyrine treatment of active rheumatic carditis have been most successful. There was prompt remission of the clinical manifestations, and the laboratory data indicated that an active rheumatic infection had been converted into an inactive one.

Further observations should be made to determine the efficacy of the aminopyrine treatment in maintaining the patient in a state of well being and the length of time the maintenance dosage must be continued.

SCHLUTZ, Chicago.

STAPHYLOCOCCUS SEPTICEMIA. P. F. STOOKEY and L. A. SCARPELLINO, South. M. J. **32**:173 (Feb.) 1939.

In a compilation of the records on 117 cases of staphylococcic septicemia from various hospitals the authors found the gross mortality to be 91.4 per cent. In 28 children less than 18 months of age the mortality was 78 per cent, and in those over 18 months of age it was 94.1 per cent. In 17 patients treated with staphylococcus antitoxin the mortality was 53 per cent.

An early diagnosis of staphylococcic septicemia should be made and treatment carried on with adequate amounts of antitoxin to prevent irreparable damage of tissues.

Although the mortality was markedly lowered by the early administration of staphylococcus antitoxin, the ideal biologic procedure has not been attained.

SCHLUTZ, Chicago.

CLINICAL ASCARIASIS IN CHILDREN. C. D. WILLIAMS, Arch. Dis. Childhood **13**:235 (Sept.) 1938.

Ascariasis causes vast morbidity and considerable mortality in children, especially in those subject to unhygienic conditions or resident in the tropics. The symptoms may include enteritis, gastroenteritis, asthma, bronchitis, pneumonia, anemia, edema, nephrosis and malnutrition. They may suggest an acute abdominal condition requiring emergency treatment. Oil of chenopodium is probably the safest and most effective means of treatment. Health education is the most effective method of prevention.

KELLY, Milwaukee.

GAS GANGRENE. C. CRAIG, M. J. Australia **2**:860 (Nov. 19) 1938.

Craig reviews 13 cases in which patients with gas gangrene were treated at the Launceston Public Hospital; 6 of the patients were cured by serum alone, 1 by amputation and serum and 4 by surgical means without serum. In the cases in which treatment with serum was successful the initial dose varied from 50,000 to 100,000 units and the total dosage from 170,000 to 250,000 units. Of the 13 patients, 9 had from 10,000 to 20,000 units of antiserum as a prophylactic dose.

GONCE, Madison, Wis.

DIAGNOSIS OF KALA-AZAR BY SEARCH FOR THE PARASITE IN THE BONE MARROW (PUNCTURE OF THE METAPHYSIAL REGION OF THE TIBIA). L. A. KARABARBOUNIS, Bull. Soc. de pédiat. de Paris **36**:157 (March) 1938.

A boy 4½ years old had fever, anemia and enlargement of the spleen and liver. He was known to have had malaria, but no malarial parasites were found in his

blood, and the administration of quinine produced no improvement in his condition. By puncture of the tibia through the metaphysial region after subperiosteal injection of procaine hydrochloride, a specimen of bone marrow was obtained which showed Leishman-Donovan bodies. Under treatment with antimony this boy made an uninterrupted recovery. BENJAMIN, Montreal, Canada.

TYPHOID IN AN INFANT FIVE MONTHS OLD. H. ESCHBACH, Bull. Soc. de pédiat. de Paris **36**:212 (April) 1938.

A boy of 5 months recovered from typhoid. The only complication was otitis media. The mother of the infant had been in contact with her brother, who apparently had typhoid ten days previous to the onset of the infant's illness. Bacillus typhosus was cultured from the infant's blood. The liver was markedly enlarged, while no enlargement of the spleen was observed.

BENJAMIN, Montreal, Canada.

SEPTICEMIA DUE TO DIPLOCOCCUS CRASSUS, SIMULATING TYPHOID. RAILLIET and GUISBOURG, Bull. Soc. de pédiat. de Paris **36**:217 (April) 1938.

Blood yielding colonies of Diplococcus crassus was obtained from a boy 1 year old in whom typhoid was suspected. BENJAMIN, Montreal, Canada.

ON THE DIAGNOSIS OF AZAR. M. B. ALEMAÑY, Bol. col. med. Camaguey **1**: **40** (Oct.-Dec.) 1938.

Marfan established the fact that nearly always splenomegaly in the newborn infant is the result of syphilis. Alemañy reports on a boy of 28 days with enlargement of the spleen. Although breast fed, the infant had constant digestive disturbances over a period of weeks and was treated with mercury inunctions in spite of negative results from serologic studies of mother and child.

When the baby's blood was examined for plasmodia, the diagnosis of malaria was made, although the course of the disease was afebrile. The mother had had malaria three years before the birth of the baby. When quinine was substituted for mercury, the nutritional state improved markedly, and the organisms disappeared from the blood. Alemañy suggests that the malaria was congenital and makes the point that splenomegaly without fever may result from malaria, as well as from syphilis. DWYER, Kansas City, Mo.

SENSITIVITY TO TUBERCULIN IN RHEUMATIC DISORDERS. O. CHIARI and R. MATRICARDI, Med. Klin. **34**:500 (April 14) 1938.

Some authors contend that rheumatic manifestations (acute polyarthritis and endocarditis) are tuberculous in origin. Chiari and Matricardi reviewed the records of 365 children aged 3 to 14 years, 295 of whom were treated for rheumatism and 70 for pleurisy at the University Children's Clinic of Vienna during the years 1932 to 1936. It was found that in children with pleurisy almost 100 per cent of the reactions to tuberculin were positive, whereas in rheumatic children only 42.4 per cent were positive. The latter figure corresponds quite closely to the 39 per cent found by Dietrich for children with scarlet fever or diphtheria. Futhermore, the incidence of sensitivity to tuberculin in rheumatic subjects is about the same as that in children in general. SIEMSEN, Chicago.

IRRITATION AND TOXIC SUSCEPTIBILITY IN THE COURSE OF RHEUMATIC INFECTION. J. DUKEN, Ztschr. f. Kinderh. **59**:593 (April 2) 1938.

Duken discusses the parallelism between tuberculosis and rheumatism. According to his hypothesis, the body is "allergized" after contact (prolonged, as a rule) with the causative organisms, and the allergic phenomena are polyarthritis, exudative multiform erythema and Schönlein-Henoch purpura. He thinks that these

manifestations may be of favorable prognostic significance in that they represent resistance rather than susceptibility. They do not, however, indicate that dissemination of toxin or bacteria from the primary focus has not occurred. Presumably tonsillectomy will be of benefit when the infection is localized in the tonsils. Just as the aggravation of tuberculosis following measles may be due to interference with allergy to tuberculin, so aggravation of rheumatism may also be due to interference with allergy. Duken thinks that it may be desirable to maintain or to induce allergy to rheumatic infection. SIEMSEN, Chicago.

A SURVEY OF INTESTINAL PARASITES IN CHINESE HOSPITAL PATIENTS IN SHANGHAI. M. N. ANDREWS, Chinese M. J. **54**:341 (Oct.) 1938.

Andrews reports observations on 5,205 fecal specimens from 2,888 patients in the Henry Lester Institute of Medical Research at Shanghai. The patients were of all ages, but the number of children included in the survey was much smaller than the number of adolescents and adults in the early decades of life. The incidence of Ascaris is increased in persons between 10 and 14 years of age. Hookworm is comparatively rare in young children, as is Trichocephalus. It is noteworthy that most of the patients are infested with more than one species of parasites. NEFF, Kansas City, Mo.

Chronic Infectious Diseases

A REVISION OF THE IMMUNO-PATHOLOGIC CONCEPT OF TUBERCULOSIS. A. BLUMBERG, South. M. J. **31**:1237 (Dec.) 1938.

Blumberg states that there is no satisfactory evidence of immunity against tuberculosis. Manifestations such as those which have been considered as successful experimental results or those which have been in gross and histologic preparations are not evidence of immunity against tuberculosis. Relative immunity is apparent rather than real. At best, a degree of tolerance to the tubercle bacillus is acquired.

Additional studies in which the majority of students of tuberculosis will cooperate are needed to solve the problem of tuberculosis. SCHLUTZ, Chicago.

CEREBRAL PARATUBERCULOSIS. R. C. COHEN and W. B. WOOD, Lancet **2**:1344 (Dec. 10) 1938.

Attention is drawn to a disturbance of the central nervous system sometimes observed in children and young persons suffering from pulmonary tuberculosis. It is distinguished from tuberculous meningitis by its fleeting character and benignity. It does not appear to be identical with the acute aseptic meningitis of Wallgren.

The leading symptoms are headache and lethargy or drowsiness. These precede or accompany the onset of fever. Physical signs are few apart from sluggishness in the reactions of the pupils and sluggishness or absence of knee jerks during the attack. In 3 instances a rash was observed—erythema nodosum, generalized simple erythema, and a mixed papular and morbilliform eruption. Except for increased pressure, the cerebrospinal fluid was normal.

The syndrome is thought to be due to exudation of a clear sterile fluid into the meninges and is considered to be of an allergic rather than of a specific nature. LANGMANN, New York.

REACTION OF CHILDREN VACCINATED WITH BCG TO TUBERCULOUS INFECTION. J. C. ETCHEVERRY, Arch. de pediat. d. Uruguay **9**:342 (June) 1938.

Observations were made on a series of 2,000 children who had received BCG vaccine during the past ten years. A comparison was made with 3,000 nonvaccinated children. The authors claim that there was a decided decrease in the morbidity and mortality from tuberculosis in the vaccinated group.

Formerly, the oral route of administration of BCG was used mainly, but since July 1937 they have used the subcutaneous route, with a dose of 800,000 bacilli in 0.5 of physiologic solution of sodium chloride. SCHLUTZ, Chicago.

CEREBROSPINAL FLUID OF SYPHILITIC CHILDREN. A. AZZI and A. FRADE, Bol. Soc. cubana de pediat. **10**:580 (Oct.) 1938.

The cerebrospinal fluid of 175 children who either had syphilitic parents or were proved to have congenital syphilis was studied in the Municipal Hospital of Habana. Fifty-seven per cent of these children had positive findings in the spinal fluid. The fluid from infants, especially those with nervous symptoms, gave more definite evidence than that from children. The Lange reaction was found useful. Azzi and Frade claim that one negative reaction does not exclude the possibility of neurosyphilis or congenital syphilis, as one has to consider that the reaction may be negative if the parents have been treated or if the neurosyphilis is of the vascular type. SCHLUTZ, Chicago.

PLEURISY AS AN ALLERGIC MANIFESTATION OF PRIMARY TUBERCULOSIS. E. FILGUEIRAS, J. de pediat. **5**:141 (June-July) 1938.

Pleurisy in a 7 year old Brazilian is presented as an allergic reaction having its origin in primary tuberculosis. The case is well studied from the clinical and roentgenologic standpoints, the conclusions being based on the evidence furnished by such study. SOTO, Habana, Cuba.

BRITTLENESS OF BONES IN SYPHILITIC NURSLING. W. MIKULOWSKI, Jahrb. f. Kinderh. **146**:274 (April) 1936.

A 9 month old child had had numerous spontaneous fractures. The roentgenograms were supposedly characteristic of rickets, but antirachitic therapy was not successful. Within five weeks after antisyphilitic therapy was started, excellent results were obtained. The noteworthy findings were positive Wassermann reactions with the mother's blood and negative reactions with the child's blood and spinal fluid despite bony changes which from the author's description could have been interpreted as syphilitic. LANDAU, Hannibal, Mo.

PROGNOSIS OF TUBERCULOSIS IN INFANTS AND CHILDREN. J. BELTLE, Ztschr. f. Kinderh. **60**:95 (Aug. 26) 1938.

A review of the literature reveals great discrepancies in mortality rates from tuberculosis especially among infants (20-75 per cent). Some authors report a mortality rate of 100 per cent for infants infected in the first three months of life. The nature of the clinical material probably accounts for the wide variations in mortality rates reported. The type and dosage of infection as well as constitutional and environmental factors influence the prognosis.

Beltle reports on 514 babies treated for tuberculosis at a sanatorium. He classifies them according to age at the time of infection and according to the type of disease. Frequent accompanying findings were pyoderma and otitis media. Follow-up study over a period of one to eight years (average, four and three-tenths years) was possible in 496 cases. In a detailed discussion Beltle includes the prognosis for different forms of the disease and for different age groups, exacerbations and deaths. He found the prognosis considerably more favorable than that reported in the literature. The mortality among infected children during the first year of life was about 8.3 per cent (about 20.6 per cent during the first six months); during the second year it was about 6 per cent and during the third to sixth years less than 1 per cent. Proper care, adequate nutrition and avoidance of intercurrent infections probably influence the prognosis more markedly for infants than for older children. Exposure may be more intimate during infancy, and the resistance of infants is probably less than that of older children. The prognosis for children

returning to homes in which a member of the family has open tuberculosis but is under proper control is apparently not much worse than that for other children. Sex has no decided influence on the prognosis. SIEMSEN, Chicago.

UNDESIRABLE TUBERCULIN REACTIONS. H. BEHRENDT, Acta pædiat. **23**:129, 1938.

Behrendt has collected from his own experience, from the literature and from the response to a questionnaire 14 instances in which the application of one or another kind of tuberculin test has been followed by a local, focal or general reaction of undesirable character. In most instances the relation of cause and effect appears to be plausible if not undeniable. The complications varied in scale of severity from a transient flare-up of an ocular, renal, glandular or pulmonary tuberculous lesion, through a profound constitutional upheaval, to fatal activation of an apparently quiescent infection. The very infrequency with which such serious reactions are recognized leads to the possibility of their occurrence being ignored or lightly glossed over. In applying a tuberculin test one should invariably commence with the smallest rather than the largest dose; states of exaggerated sensitivity should be kept prominently in mind; repeated testing of known positive reactors should be avoided. McCUNE, New York.

Diseases of Blood, Heart and Blood Vessels and Spleen

RADIOLOGIC AIDS IN THE DIAGNOSIS OF HEART DISEASE IN CHILDREN: A REVIEW. E. G. LAWLER and G. A. HELLMUTH, Illinois M. J. **75**:61 (Jan.) 1939.

This review is so comprehensive and detailed that it does not permit adequate abstracting. The authors conclude that the visualization of the cardiac silhouette by means of the roentgen ray, although not new, is now beginning to be recognized as an important aid in the diagnosis of heart disease in children. The roentgenologic examination usually gives only confirmatory evidence of heart disease, but it may add useful and interesting information for the diagnosis, prognosis and management of heart disease in the child. BARBOUR, Peoria, Ill.

HAEMATOCRIT DETERMINATIONS IN NORMAL AND ABNORMAL BLOOD. J. A. McLEAN, M. J. Australia **2**:770 (Nov. 5) 1938.

The hematocrit method is described. A Hearson centrifuge, driven at a speed of 2,500 revolutions per minute, gave a constant value for corpuscular volume after one hour's centrifugation. Detailed determinations in a series of 55 normal persons were substantially the same as the values obtained in America and England. The method was applied to the diagnosis of various blood diseases, and it is recommended as a ready means of differentiating between hyperchromic macrocytic and hypochromic microcytic anemia. GONCE, Madison, Wis.

BLOOD TRANSFUSION IN PEDIATRIC THERAPY. A. IANCU and C. OPRISIU, Med. inf. **1**:22 (Jan.) 1939.

Iancu and Oprisiu take up the problem of blood transfusion, dwelling especially on the classic opinions which should be taken into consideration and bringing out the accidents resulting from transfusion. In the researches which they carried out on infants with digestive disturbances they determined the action of the transfusion of blood on the nitrogen elements of the blood serum and noted an increase in total nitrogen, an increase in polypeptids and a decrease in the serum-globulin ratio. It is necessary to perform examinations to establish compatibility of plasma as one previously established compatibility of globulin. Such a procedure will be of the greatest value in the elimination of risks from this therapeutic measure.

FROM THE AUTHORS' SUMMARY.

THE ELECTROCARDIOGRAM TAKEN FROM THE WALL OF THE NORMAL CHEST IN CHILDHOOD. E. LEPESCHKIN, Arch. f. Kreislaufforsch. **3**:321 (Dec.) 1938.

Experience in the University Children's Hospital at Vienna has shown that myocardial damage sometimes may be detected earlier by making the electrocardiogram with a lead from the wall of the chest than by making it only with leads from the extremities as formerly was done. However, with normal children the lead from the wall of the chest sometimes gives tracings which according to experience with adults have to be regarded as pathologic. For this reason 50 children between 2 weeks and 15 years of age, who were normal and healthy according to cardiac findings, were selected, and from all these children electrocardiograms were taken with leads from ten to twenty different places on the wall of the chest, from the left leg and from the right arm. The chest wall locations were checked by roentgenograms and each electrocardiographic figure was placed at the roentgenogram, exactly at the same place at which the electrode had been fixed.

The first wave of the anterior chest wall electrocardiogram is formed by an initial + and a following — wave. Since the wall of the right ventricle during the first year of life is larger than at later ages the + wave with infants is greatest at the right of the sternum; however, with older children, as with adults, it is greatest at the apical region.

The T wave also is different as between children and adults. The more the interventricular borderline runs to the left the younger is the child, a fact by which the different appearances of the T wave in children of various ages is explained. A negative T wave of the chest wall electrocardiogram is not necessarily to be regarded as a sign of myocardial damage. However, when during the course of a disease the electrocardiograms are taken with exactly the same position of the electrode and the T wave shows a shift to the "—" while there is no change in the position of the heart (e. g., in pneumothorax) surely myocardial damage is demonstrated.

ARON, Chicago.

GLOMERULOTUBULAR NEPHROPATHY IN SCHOENLEIN-HENOCH PURPURA. H. ZOTHE, Zentralbl. f. inn. Med. **59**:657 (Sept.) 1938.

Zothe reports 2 cases of Schoenlein-Henoch purpura, in which hematuria and albuminuria were noted. One of the patients, a boy 11 years old, succumbed. Postmortem examination of the kidneys showed chronic glomerulonephritis with a high degree of lipoid nephrosis.

ARON, Chicago.

A METHOD OF COUNTING THROMBOCYTES IN THE CHILD. E. LORENZ, Ztschr. f. Kinderh. **60**:142 (Aug. 26) 1938.

On the basis of clinical and experimental experience Lorenz regards Jürgens method of counting thrombocytes (blood counting chamber) much superior to that of Tonio (smear), especially in the study of pathologic conditions. With the former method values averaged 551,000; with the latter, 360,000. The lesser accuracy of the Tonio method is attributable mainly to the destruction of platelets (especially smaller ones) during the preparation of the smears.

SIEMSEN, Chicago.

INVESTIGATION CONCERNING THE QT INTERVAL OF THE ELECTROCARDIOGRAM IN DIPHTHERIA OF CHILDREN. HANS BOCK, Ztschr. f. Kreislaufforsch. **30**:761 (Oct.) 1938.

The length of the QT interval corresponding to the time of the electrical systole during the course of diphtheria was studied. In 1,200 electrocardiograms it was ascertained that an increase in length of the QT distance during the course of diphtheria is surprisingly frequent. Two main types are distinguished:

1. A minor increase in length originating in cases of mild and of moderately severe diphtheria, usually after the second week. It persists far into convalescence. In cases of severe diphtheria this increase is encountered in the first week and persists a long time.

2. A pronounced increase in length originating mostly in the first week, less frequently during the second week. This alteration disappears after a while and is found much more frequently in cases of severe diphtheria than in cases of mild diphtheria.

The increase in length of the QT interval is regarded as a sign of diphtheritic myocardial damage. The minor increase in length is apparently of no importance. The extreme increase in length is a grave sign. However, even patients with this sign recover, and therefore the prognosis is not hopeless.

ARON, Chicago.

COARCTATION OF THE AORTA: REPORT OF A CASE. J. S. MCNAIR, Chinese M. J. **54**:331 (Oct.) 1938.

A boy of 11 years presented himself at the outpatient department of the medical college at Mukden, China, with a complaint of dull pain at the umbilicus, loss of appetite and failure to maintain weight. Examination of the abdomen revealed a pulsating superior epigastric artery. The blood pressure was high. The absence of a femoral pulse, the physical signs, the roentgenograms of the chest and the erosion of the under surface of the fifth rib on the right side and of the sixth and seventh ribs on the left suggested the diagnosis. Coarctation is not impossible to recognize in the living subject.

NEFF, Kansas City, Mo.

SEDIMENTATION RATES IN NONTUBERCULOUS DISEASES. K. MURAKAMI, Acta pædiat. japon. **44**:1396 (Sept.) 1938.

Murakami made 1,760 determinations of the sedimentation rate of erythrocytes in 968 children suffering from various diseases exclusive of tuberculosis. The rate was highest in infants with any of the following diseases: congenital syphilis, empyema, croupous pneumonia, bronchopneumonia, aplastic anemia, myeloid leukemia, congenital obstruction of the bile duct, acute nephritis, nephrosis, pyelocystitis, sepsis, Weil's disease, malignant tumors and epidemic encephalitis. It was normal in infants with any of the following: pertussis, acute dyspepsia, dyspeptic toxicosis, malnutrition, autointoxication, congenital heart disease, lead poisoning, infantile beriberi, infantile scurvy, rickets, noninflammatory diseases of the nervous system, endocrine disorders, spontaneous hemoglobinuria and exudative diathesis.

KATO, Chicago.

THROMBOSIS OF THE SPLENIC VEIN (SO-CALLED SPLENIC VENOUS STENOSIS). K. KAWASHIMA and K. YAMADA, Acta pædiat. japon. **44**:1777 (Nov.) 1938.

A case of thrombosis of the splenic vein in a boy 4 years and 6 months old is reported, with the observations at autopsy. The chief clinical and laboratory signs were hematemesis, splenomegaly, anemia, leukopenia and thrombopenia. Autopsy revealed thrombosis in the inferior mesenteric vein. The spleen showed marked hyperplasia of capsular tissue, atrophy and diminution in number of follicles and remarkable increase in connective tissue and elastic fibers. Although there was evidence of fibrous changes, no typical fibrosis was noted. Yellowish brown pigments were abundant in the pulp. No hepatic cirrhosis, such as that found in Banti's disease, was present. Splenectomy in an early stage of the disease results in recovery in 60 per cent of cases.

KATO, Chicago.

WHITE BLOOD CELL PICTURE DURING THE FIRST YEAR OF LIFE, ESPECIALLY WITH REGARD TO ITS COURSE. J. H. MAGNUSSON, Acta pædiat. **23**:14, 1938.

This investigation was made for the purpose of obtaining normal standards with which to compare white blood cell counts of premature infants. Forty-seven healthy infants were selected; all were born normally of healthy mothers and weighed between 3,000 and 3,500 Gm. at birth. All were fed in an approved fashion. None suffered serious infections during the period embraced by the study; none manifested even trivial infection at the time the blood counts were made; absence of infection was confirmed by normal erythrocyte sedimentation rates. The quantitative hematologic technic was carefully standardized. Sixteen observations were made during the third week of life, twenty during the eleventh week, twenty between the twenty-third and twenty-fifth and twenty between the forty-ninth and fifty-second weeks. Standard statistical methods for small number analysis were employed in assessing the results.

The total number of leukocytes was found to average 14,180 at the third week of age; it fell to 10,790 at the eleventh week, then rose again to 13,410 by the twenty-third to twenty-fifth week, where it remained until the end of the first year. The total leukocyte curve paralleled those representing the red blood cell count and the hemoglobin concentration. The form of the curve for the total white blood cell count was determined principally by the changing number of granular cells; the concentration of lymphocytes and monocytes remained relatively constant.

In agreement with other studies, the total and differential leukocyte counts were found to exhibit great variability. The data demonstrate the difficulty of interpreting a single white cell count on blood of an infant. A tabular summary of comparable studies by other investigators is inserted; the bibliography lists 60 titles.

McCUNE, New York.

Diseases of Nose, Throat and Ear

OTITIS MEDIA FROM THE PAEDIATRICIAN'S VIEWPOINT. G. A. CAMPBELL, Canad. M. A. J. **40**:146 (Feb.) 1939.

Campbell advises local treatment with chlorbutanol, ephedrine, glycerin and water for twenty-four to forty-eight hours in the average case of otitis media. If no improvement has been observed by that time, he advises myringotomy.

If the condition is in the acute stage, sulfanilamide is used and has been found to be effective in shortening the course of otitis and preventing mastoid complications. A concentration of 4 mg. per hundred cubic centimeters of blood is maintained.

Toxic symptoms were rare.

During 1936 and 1937 the average number of days of hospitalization in cases of otitis was 24.15 and the incidence of complications 8.2 per cent. During 1937 and 1938, with routine use of sulfanilamide, the average duration of hospitalization was reduced to 8.07 days and the incidence of complications to 4.1 per cent.

Campbell stresses the importance of latent mastoiditis as a cause of fatal marasmus; 53 per cent of all children who died in the hospital showed purulent mastoiditis at autopsy.

MOORE, Omaha.

FOUR CASES OF MASTOIDITIS WITHOUT MIDDLE EAR INVOLVEMENT. R. FRANCIS, M. J. Australia **2**:692 (Oct. 22) 1938.

Francis reports 4 cases of primary mastoiditis. The patients were 2 adults and 2 children of 14 years each.

GONCE, Madison, Wis.

PARANASAL SINUSES IN CHILDREN. A. BOWEN-DAVIES, Proc. Roy. Soc. Med. **31**:1411 (Oct.) 1938.

Bowen-Davies took 55 children between the ages of 5 and 14 years and made a routine examination of each. A roentgenogram was taken, the nose was cocainized and swabbed, and both antrums were punctured. The washings were cultured and the antrums filled with iodized poppyseed oil 40 per cent. Further roentgenograms were taken at once and at intervals of a week or so until the antrums were clear of iodized oil. The volume of iodized oil and the time it took to disappear were recorded. Organisms were found in the antrums of 23. Mucopus was found in the antrums of 19 patients, and cultures of the mucopus from 6 of these proved to be sterile. The organisms found in the antrums, both those in which the mucopus was infected and those in which it was sterile, were similar to those present in the nose. Five tables are given listing the organisms found in the various cases, together with a series of roentgenograms showing the progress of the evacuation of the iodized oil. In all cases improvement followed the injection of iodized oil, not only in the clinical condition of the patient but also in the roentgenographic appearance of the antrums. Local treatment is of established value, and the removal of tonsils and adenoids may be advisable. An abundance of fresh air, an adequate diet and a plentiful supply of vitamins may do a great deal to prevent sinusitis in children. WILLIAMSON, New Orleans.

SEDIMENTATION REACTION IN OTITIS MEDIA AND ITS COMPLICATIONS. P. FRENCKNER, Acta oto-laryng. **26**:309, 1938.

Frenckner, together with Hamberger, followed all the cases of otitis media at the Sabbatsberg Clinic for a period of three years. His material consists of 1,341 cases of otitis or otitis with otitic complications uncomplicated by the presence of any other disease which might affect the sedimentation rate to any marked degree. He also studied 147 additional cases in which otitis was complicated by such diseases as angina, bronchopneumonia, nephritis and polyarthritis. As a rule, the sedimentation rate was taken every second day throughout the entire course of the disease. The studies were made partly according to Westergren's original method, called the "macro" method, and partly by Strom's "micro" method, blood being taken from the finger tip. In many cases parallel tests with the two methods were made, and the author found them fairly consistent.

He found little disturbance in the sedimentation rate in cases of chronic otitis, with or without complications.

In cases of acute otitis in children the sedimentation rate rises in the first week or first two weeks and then gradually falls. In cases of acute mastoiditis there is a speedy rise in the sedimentation rate, which then remains stationary for some weeks. In cases of virulent mastoiditis or when a complication is threatening there is no stationary period but rather a continued rise. If this takes place, the author advises earlier operation, even in the absence of other symptoms.

The formation of abscesses or enclosed ostitic foci in the zygomatic or digastric region or in the pars petrosa causes a rise in the sedimentation rate, as do sinus thrombosis and meningitis. Labyrinthitis has little effect on the sedimentation rate.

A rise in the sedimentation rate accompanying or preceding a rise in the patient's temperature in the course of otitis, either before or after operation, is often due to an otitic complication. When the complicating condition is angina or some other intercurrent febrile disease, there is always first a rise in the temperature and two to four days later a rise in the sedimentation rate.

A sedimentation rate of over 100 in an adult indicates almost without exception that the condition is operable. The same conclusion can be drawn with great probability in respect to children under 15 and with considerable probability in respect to infants. GROVE, Milwaukee. [ARCH. OTOLARYNG.]

Diseases of Lungs, Pleura and Mediastinum

BILATERAL LOBECTOMY FOR BRONCHIECTASIS. D. E. ROSS, Canad. M. A. J. **39**:549 (Dec.) 1938.

Two cases of bilateral lobectomy are reported. One patient was a girl aged 5 years and the other a girl aged 6 years. The observations in these 2 cases indicate that bilateral lobectomy can be performed without leaving any ill effects. Altogether, 11 cases of bilateral lobectomy have been reported, with a single death, or a mortality rate of 9.9 per cent, which approximates that of unilateral lobectomy. The most important single factor affecting the death rate would seem to be the stage of the disease at which the operation is performed. The time of choice is before anaerobic organisms are present; i. e., in Archibald's so-called second stage.

A preoperative dose of scopolamine and morphine was given each patient, and the operation was done with the patient under spinal anesthesia.

MOORE, Omaha.

THE RHEUMATIC LUNG. G. HADFIELD, Lancet **2**:710 (Sept. 24) 1938.

"Rheumatic lung" is a noncommittal designation for a highly characteristic variety of massive pulmonary consolidation which occasionally complicates rheumatic carditis in its acute phase. Consolidation is always massive in fatal cases. While it may involve almost the whole of both lungs, it is commonly unilateral and in a minority is strictly confined to the upper lobe of the right lung. The consolidated lung has an india rubber consistency.

The primary lesion responsible for the consolidation is widespread fibrinous alveolitis. This is followed by cellular infiltration, mononuclear in type, relatively slow in development, but eventually becoming copious and diffuse.

In fatal cases this primary lesion is complicated by hyaline pseudomembrane formation in most of the alveolar ducts in the consolidated lung.

As in other varieties of pneumonitis, this process takes place in lungs in which the finest ramifications of the airway contain viscid albuminous exudate.

The dyspnea which initiates membrane production in the rheumatic lungs is probably cardiac in origin.

Hyaline membranes in the alveoli have been described in influenza, in pneumonic plague, in acute streptococcic pneumonia, in acute tuberculous pneumonia and in asphyxiation from aspiration of amniotic fluid.

LANGMANN, New York.

LUNG DISEASES: PULMONARY TUBERCULOSIS, MILD BRONCHIECTASIS, STAPHYLOCOCCAL EMPYEMA AND DIAPHRAGMATIC HERNIA INTO THORAX. C. MCNEIL, Tr. Med.-Chir. Soc. Edinburgh, 1938, p. 183; in Edinburgh M. J., October, 1938.

McNeil presented a case of each of the thoracic disturbances listed in the title at a clinical meeting.

A 10 year old girl clearly showed local tuberculous disease of the right lung in the roentgen film. There were a few large cavities surrounded by tissue that was progressively tuberculous. The disease had been latent although advanced. What finally brought her to the hospital were repeated hematemeses. Tubercle bacilli were found in the vomitus. Hospitalization for several months resulted in clearing up of the cough, increase in weight and a generally good condition though ultimate good results could not be expected.

A boy of 5 years had mild bronchial dilatation bilaterally, with some fibrosis of the lung on the right side. The disease had been present about three years and had followed measles and whooping cough with pneumonia. Such severe acute illness injured the bronchial walls. The child had remained in a good general condition. His treatment was very simple—postural coughing, with attention to the condition of the upper respiratory tract.

In an infant of 7 months there was pus as well as air in the chest, and the organism was the staphylococcus. This type of pneumonia is fatal and is usually accompanied by suppurative pleurisy. In this infant there was primary acute pleurisy where a superficial staphylococcic abscess had ruptured into the pleura without producing ill health until the time of admission. Then dulness and fluid were present in the base of the right lung, and the organisms were found in the pus. The presence of air with the fluid caused positive pressure with leakage of the pus along the needle thrust. This child, it was stated, would recover by aspiration without drainage.

A 4 month old baby was brought into the hospital suffering from a respiratory syndrome—faintness of breath sounds and dulness at the base of the right lung. A small amount of clear sterile fluid was withdrawn from the pleural region at the base of the right lung. The roentgen film did not help until barium sulfate was given, which showed the stomach above the diaphragm, an observation sufficient to establish the diagnosis of hernia. NEFF, Kansas City, Mo.

ACTION OF INTRAPLEURAL INJECTIONS OF HYPERTONIC SOLUTIONS OF SUGAR IN PLEURITIS EXSUDATIVA AND IN EMPYEMA. BAUER, Ztschr. f. d. ges. exper. Med. **104**:364 (Oct.) 1938.

In 6 cases of empyema after aspiration of the exudate 40 to 60 cc. of 50 per cent solution of dextrose was injected intrapleurally in order to produce osmotic action on the pleura. However, even when the pleura was severely affected, the sugar was absorbed quickly, in contrast to the nitrogen split products, which remain in the pleural cavity a rather long time. Therefore hardly any therapeutic effect was seen. ARON, Chicago.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

CHOLECYSTITIS AND CHOLELITHIASIS IN CHILDHOOD. I. P. SOBEL, Arch. Pediat. **55**:669 (Nov.) 1938.

The case of a 6 year old girl is reported, and the literature on the subject is reviewed. ORR, Buffalo.

SALMONELLA PANAMA. F. SCHIFF, J. A. M. A. **111**:2458 (Dec. 31) 1938.

A report is made of the cases of 4 infants ill with diarrhea. Cultures of the stools in 3 cases and a postmortem culture of the blood in 1 revealed Salmonella of the Panama type as the causative agent. It was identified by bacteriologic and serologic examination. HEERSMA, Kalamazoo, Mich.

TREATMENT OF DIARRHEA IN CHILDREN. A. G. MITCHELL, J. A. M. A. **112**:114 (Jan. 14) 1939.

After discussing briefly the cause of diarrhea and the clinical and pathologic observations, Mitchell covers the treatment especially from the standpoint of the drugs used. The dietary management and the prevention of acidosis and anhydremia are included. HEERSMA, Kalamazoo, Mich.

ACUTE INTUSSUSCEPTION IN CHILDREN. C. P. G. WAKELEY and F. R. B. ATKINSON, Brit. J. Child. Dis. **35**:241 (Oct.-Dec.) 1938.

This report is based on 121 cases personally observed by Wakeley. Of the patients, 70 per cent were males, and 72 were under 1 year of age. The youngest was a girl aged 3 weeks.

The most constant feature in these cases was enlargement of the glands in the root of the mesentery and in the ileocecal angle, together with a preponderance of lymphoid tissue in the terminal part of the ileum and around the orifice of the ileocecal valve. This lymphoid tissue acting as a foreign body may cause increased peristalsis of the intestines, which at times culminates in intussusception.

The types of intussusception encountered in the patients were: ileocecal in 67; ileocolic in 41; enteric in 6; enteric and ileocecal in 5; enteric and ileocolic in 2.

Twelve of the patients died after operation (10 per cent); 10 were under 1 year and the other 2 were between 1 and 2 years of age. LANGMANN, New York.

HERNIA OF THE VERMIFORM APPENDIX. C. P. G. WAKELEY, Lancet **2**:1282 (Dec. 3) 1938.

• Sixteen cases of hernia of the vermiform appendix are reported, 12 associated with inguinal, 3 with femoral and 1 with umbilical hernia. In 3 cases retrograde strangulation was found. LANGMANN, New York.

CONGENITAL HYPERTROPHIC STENOSIS OF PYLORUS. L. THATCHER, Tr. Med-Chir. Soc. Edinburgh, 1938, p. 187; in Edinburgh M. J., October 1938.

Two babies were shown who began to have symptoms of stenosis of the pylorus on the fourteenth day of life. They had received a preliminary administration of salt solution and a dose of atropine methyl nitrate before each feeding. The formula had been acid-separated milk, and there had been gastric lavage daily. As a result the vomiting stopped within ten days, and there was no residue in the stomach at the end of three hours. Thatcher believes that it is not always possible to select the infants who will do well with this preparation of atropine, but he does think that treatment should be started at the very onset of the symptoms and that surgical assistance is indicated when the obstruction does not disappear within a few days. NEFF, Kansas City, Mo.

IMPETIGINOUS STOMATITIS. J. NICOLAS, J. ROUSSET and J. RACOUCHOT, Bull. Soc. de dermat. et syph. **45**:499 (April) 1938.

The authors call attention to pyogenic stomatitis associated with impetigo. Three cases in the same family are cited. The use of 1 per cent methylthionine chloride (methylene blue) and 10 per cent silver nitrate resulted in rapid improvement. LAYMON, Minneapolis. [ARCH. DERMAT. & SYPH.]

RIGHT DIAPHRAGMATIC HERNIA. G. PAISSEAU, G. GUÉNAUX and J. GAUTIER, Bull. Soc. de pédiat. de Paris **35**:561 (Oct.) 1937.

A child 10 years old who had a positive tuberculin test was thought to have a pulmonary lesion at the base of the right lung. Investigation revealed that a congenital diaphragmatic hernia was present which involved the cecum and the ascending colon. BENJAMIN, Montreal, Canada.

TWENTY CASES OF FECAL INCONTINENCE IN CHILDREN. G. HEUYER and ROUDINESCO, Bull. Soc. de pédiat. de Paris **35**:704 (Dec.) 1937.

Of 20 children who had encopresis, associated in some with enuresis, 60 per cent were considered to be syphilitic. It is stated that syphilis plays an important role in this condition. In the discussion, megacolon, constipation, relaxation of the anal sphincter and spasm of the anal sphincter are reported to have been present in cases described by various observers. No mention is made of faulty mental hygiene. BENJAMIN, Montreal, Canada.

CONGENITAL MEGACOLON IN A BOY OF TEN YEARS; IMPROVEMENT FOLLOWING AN OPERATION ON THE SYMPATHETIC NERVOUS SYSTEM. C. LAUNAY and R. M. D'AUBIGNÉ, Bull. Soc. de pédiat. de Paris **36**:124 (March) 1938.

A 10 year old boy with megacolon had been subjected to an operation which consisted in resection of the inferior mesenteric plexus and presacral nerve. Four months later the abdomen was still large, though smaller than previously. His general condition had improved. BENJAMIN, Montreal, Canada.

CONGENITAL MICROCOLON. J. R. ABDALA and others, Arch. argent. de pediat. **9**:33 (Jan.) 1938.

The authors present a case of congenital microcolon, the third in their series. A complete pathologic description is given. They believe that in this case the hypoplasia of the colon was secondary to an obstruction in the terminal part of the ileum and ileocecal valve. SCHLUTZ, Chicago.

SALMONELLA ENTERITIS IN INFANTS. J. LORENZO and DEAL, Arch. Child. Hosp. Roberto del Rio **7**:215 (Dec.) 1937.

Lorenzo and Deal describe 12 cases of enteritis due to Salmonella, with 6 deaths. The infection occurs most frequently in malnourished infants who have been prematurely weaned. There is no specific treatment. The disease is a septicemia in which the reticuloendothelial system, especially the spleen, plays an important role. Dehydration is severe, and the lesions are found mainly in the small intestine. SCHLUTZ, Chicago.

URGENT EARLY DIAGNOSES IN LIFE-THREATENING DISEASES OF THE ADOMINAL ORGANS IN CHILDHOOD. A. LOESCHKE, Med. Klin. **34**:538 (April 22) 1938.

Appendicitis, intussusception, alimentary intoxication and toxic enteritis (Ruhr) are discussed. As evidence of appendicitis, tenderness on percussion and diminution of the abdominal reflex over the right lower quadrant of the abdomen are regarded as important. SIEMSEN, Chicago.

APPENDICITIS IN CHILDHOOD. A. OBERNIEDERMAYR, Med. Klin. **34**:541 (April 22) 1938.

Oberniedermayr discusses the diagnosis of appendicitis in children and the differential diagnosis. He stresses an approach that will tend to enlist the cooperation of the child for a satisfactory examination. Observation and repeated examination may be necessary. Surgical treatment is discussed. Avertin with amylene hydrate is the anesthetic of choice, to be administered by rectum.

SIEMSEN, Chicago.

VALUE OF THE RAW APPLE TREATMENT. R. BARANSKI and T. LEWENFISZOWA, Pediatria polska **18**:207 (April) 1938.

Baranski and Lewenfiszowa have treated over 40 children for gastrointestinal disturbance with raw apple. The results were very unsatisfactory, particularly in those with toxic colitis. The banana treatment was just as unsatisfactory. However, in conclusion the authors claim that in exceptional cases a fruit diet is indicated and that results are encouraging. KRUPINSKI, Chicago.

A CASE OF NOMA WITH RECOVERY FOLLOWING ADMINISTRATION OF QUININE. ILCHENKO, Vrach. delo **20**:151, 1938.

The noma occurred in an 8 year old girl in the course of influenzal pneumonia and was so extensive that the surgeons refused to undertake any operative pro-

cedure. In view of the grave prognosis given, the parents decided to take the child home. Ilchenko, however, was able to administer to her before her discharge two injections of a 10 per cent solution of quinine in doses of 3 cc. each. A mouth wash of potassium permanganate solution was likewise recommended. Two weeks later the child came to the clinic completely recovered. The author, not having had the opportunity to try this form of therapy in a larger series of cases, urges other physicians to investigate along this line. BODER, Los Angeles.

Nervous Diseases

TICS IN CHILDHOOD. M. A. BRESCIA, Arch. Pediat. **55**:703 (Nov.) 1938.

In the case reported the tic was due to defective vision. ORR, Buffalo.

ETIOLOGY OF CHOREA: ITS RELATION TO RHEUMATIC FEVER AND HEART DISEASE. S. J. USHER, Canad. M. A. J. **39**:565 (Dec.) 1938.

Usher presents the results of his study of 105 patients who were admitted to the rheumatism pavilion of the Children's Memorial Hospital of Montreal for treatment of chorea. In 56 the condition was purely chorea; i. e., the patients showed no rheumatic symptoms. In 49 chorea was mixed with rheumatic symptoms.

If the patients with infected tonsils and repeated infections of the upper respiratory tract were omitted from the group with pure chorea, only 14 per cent showed evidence of endocarditis. In the group with chorea and rheumatic symptoms 65 per cent showed heart disease.

Usher believes that valvular heart disease in patients with chorea is due not to the chorea per se but to intercurrent attacks of polyarthritis or severe infections of the upper respiratory tract associated with infection of the tonsils. He also believes that more should be made of the psychic element and that removal of this disturbing condition will do more to prevent recurrences than removal of foci of infection. MOORE, Omaha.

SULFANILAMIDE IN THE TREATMENT OF ACUTE INFECTIONS OF THE CENTRAL NERVOUS SYSTEM. J. B. NEAL, E. APPELBAUM and H. W. JACKSON, M. Clin. North America **22**:1419 (Sept.) 1938.

The value of sulfanilamide in the treatment of virus diseases is problematic. Also, its value in the treatment of meningitis due to the staphylococcus, the influenza bacillus or the nonhemolytic streptococcus is doubtful. The pneumococcus likewise seems resistant to sulfanilamide since of 25 persons with pneumococcic meningitis in whom it was employed, only 4 recovered. While the experience of the authors with sulfanilamide in the treatment of meningococcic meningitis has been limited and the case fatality high, they believe that it has a favorable effect on the disease and may well replace intravenous use of serum in cases of meningococcemia with or without meningitis. Most encouraging results were obtained in the treatment of meningitis due to infection with the hemolytic streptococcus. During an earlier period of more than twenty-six years the authors observed 274 cases of the various forms of streptococcic meningitis; recovery occurred in only 15 cases, 9 of which were definitely cases of infection with the hemolytic type of streptococcus. Since 1937 they have treated 19 patients with sulfanilamide, with 14 recoveries and 5 deaths.

The preparations used were prontosil soluble (disodium 4-sulfonamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3′, 6′ disulfonate, now known as neoprontosil) intramuscularly, sulfanilamide orally and at times an 0.8 per cent solution of sulfanilamide crystals intraspinally. As a rule, 5 cc. or less of neoprontosil was given to younger children and 10 cc. every four hours to older children and adults. In addition, from 5 to 15 grains (0.3 to 1.0 Gm.) sulfanila-

mide was given by mouth every six hours. This combination seems to be more effective than either preparation alone. The advantage of giving the drug intraspinally is open to question. The large doses advocated by some do not seem to be necessary. The authors emphasize that in the treatment of meningitis caused by the hemolytic streptococcus it is of great importance that the primary foci of infection be removed.

EUGENE H. SMITH, Ogden, Utah.

SPONTANEOUS SUBARACHNOID HEMORRHAGE IN CHILDREN. H. G. MILLER, Arch. Dis. Childhood **13**:258 (Sept.) 1938.

Spontaneous subarachnoid hemorrhage is described in 5 children between the ages of 2 and 12 years, fatal in 2 and confirmed by lumbar puncture in all. The children presented various clinical pictures, which were strictly comparable to those known to occur in adults with this disease. One patient had a facial hemangioma, which led to a suspicion of some similar intracranial lesion as a source of the hemorrhage, and in 3 of the other 4 patients the presence of an aneurysm, probably congenital, was suspected. The role of effort in the provocation of the attack and the frequency of premonitory symptoms are illustrated, and the pyrexial phenomena associated with the hemorrhage are shown to be somewhat inconstant as compared with the findings in adults.

KELLY, Milwaukee.

HYDATID CYST OF THE SPINAL CANAL SUCCESSFULLY TREATED BY OPERATION. J. S. Y. ROGERS, Arch. Dis. Childhood **13**:269 (Sept.) 1938.

A case is reported of hydatid cyst in the spinal canal of a child; pressure on the cord had produced paresis and parasthesia of the lower limbs. Operative treatment by laminectomy resulted in a complete cure.

KELLY, Milwaukee.

CENTRAL LOBAR LEUKOENCEPHALOSCLEROSIS, SYMMETRICAL, PRIMARY AND PROGRESSIVE. A. GAREISO, J. P. KÄFER, E. A. PEDACE and L. RASCOVSKY, Rev. méd. latino-am. **24**:121 (Nov.) 1938.

The authors review briefly the cases of Schilder's disease reported from South America and report a case in a girl aged 9 years. One and one-half years before the illness the girl had a febrile disturbance in which she became comatose for two days. A few months later she had measles. One year later difficulties in behavior, loss of attention, loss of memory and more pronounced psychic disturbances appeared. Headache, progressive loss of vision, motor disturbances, choreic manifestations, hypotonia, optic atrophy, amaurosis, and finally death from a pulmonary complication characterized the course of the disease. A detailed histologic examination is reported, illustrated with 14 photomicrographs.

DWYER, Kansas City, Mo.

OUTCOME OF CONVULSIONS IN EARLY CHILDHOOD AND EFFECT OF ROENTGEN RAYS. E. WITTERMANN, Ztschr. f. Kinderh. **60**:9, 1938.

Several authors have reported favorable results in the treatment of organic epilepsy with roentgen rays. Wittermann reports 31 cases individually, in about half of which there were signs of cerebral disturbance. Even in the absence of positive signs, pathologic changes may be present in silent areas. An early onset (average, about 2½ years) of the convulsions and cessation of mental development or regression of mentality after the onset are regarded as evidence of the organic nature of the convulsions. The 31 patients are divided into two groups. In group 1 dementia had progressed to a rather marked degree, and the results of roentgen therapy were poor. Group 2 was subdivided into a series of patients to whom roentgen therapy was not given, and a series to whom it was given. In this group the results of roentgen therapy were definitely encouraging. The

possibility of spontaneous remission is militated against by the unfavorable course of the patients not treated. Wittermann regards the triad of convulsions, dementia and signs of progressive cerebral deterioration as an indication for roentgen therapy. Early treatment is important. SIEMSEN, Chicago.

ETIOLOGIC FACTORS IN CHOREA MINOR. G. EDGREN, Acta med. Scandinav. **96**:43 (June 30) 1938.

Edgren points out that the most widely accepted opinion concerning the cause of chorea minor is that it has some connection with a rheumatic infection. Bacteriologic examinations of the brain, spinal fluid and blood of patients with chorea minor have yielded diplococci, staphylococci and streptococci. The pathoanatomic aspects of the brain vary; embolisms, congestion and small hemorrhagic foci have been observed. Moreover, attacks of chorea minor have been known to alternate with attacks of acute polyarthritis or endocarditis, and infections of the throat, measles, scarlet fever and influenza have been suspected of connection with chorea minor. Other investigators have suggested dysfunction of the parathyroid glands and psychic or physical traumas as causal factors of chorea minor. The majority of investigators regard hereditary predisposition as an important factor in the development of chorea minor, and Edgren reports the case of a girl with chorea minor whose siblings were also subject to these attacks. Moreover, the mother of these siblings had had attacks of chorea gravidarum in the course of several pregnancies. The erythrocytic sedimentation speed of a large percentage of patients with chorea minor was either normal or slightly increased. Edgren reaches the conclusion that the cause of chorea minor has not been fully explained. Many factors indicate that chorea minor is not a definite disease entity but a syndrome with various causes. Hereditary predisposition probably plays an important etiologic role. EDITOR'S ABSTRACT. [ARCH. NEUROL. & PSYCHIAT.]

Psychology and Psychiatry

PSYCHIATRY AND PEDIATRICS. J. ZAHORSKY, Arch. Pediat. **55**:717 (Nov.) 1938.

Zahorsky questions the attitude sometimes shown in hospitals that the sick child should not be pampered and spoiled. Making a sick child comfortable and happy is good pediatrics. Letting a mother care for her child in her own way, guided by her own intelligence and motivated by mother love, is also good pediatrics. ORR, Buffalo.

SOME OBSERVATIONS ON THE DEPTH AND NERVE-CELL CONTENT OF THE SUPRAGRANULAR CORTEX IN NORMAL AND MENTALLY DEFECTIVE PERSONS. R. M. NORMAN, J. Neurol. & Psychiat. **1**:198 (July) 1938.

Norman examined microscopic sections from the brains of 30 normal persons and of 30 mentally defective persons whose brains exhibited no gross pathologic changes. Three cortical areas were selected for examination: (1) Bolton's "visuopsychic" area (area O. A. of von Economo), (2) the frontal pole (area F. E. of von Economo) and (3) the supramarginal gyrus (area P. F. of von Economo). Micrometric measurements of the supragranular cortex failed to reveal any significant difference in mean depth of cortex between normal and defective persons, thus disproving Bolton's contention that amentia is associated with specific reduction in the supragranular cortex. However, a series of counts of neuron cells made in the middle of this pyramidal cell lamina disclosed two abnormal processes: (*a*) excessive crowding of the nerve cell bodies, leading to an increased cell count, and (*b*) undue sparseness, leading to a low cell count. In the defective persons there was greater variability in the average nerve cell contents of different sections as well as in the distribution of cells within the same section of the brain than in normal persons. There was no significant difference between persons with mon-

golism and defective persons without mongolism in regard to mean cell content or variability in distribution of nerve cells. Norman regards crowding of nerve cell bodies as characteristic of the defective brain, interpreting it as a sign of inhibited development. On the other hand, relative deficiency of nerve cells is observed also in normal brains, although it is more frequent in defective brains. The sparseness of nerve cells may be due to faulty development or to degenerative phenomena. In general, the investigation supports the view that amentia is commonly associated with structural abnormalities of the parts of the neopallium which have been most recently acquired.

MALAMUD, Ann Arbor, Mich. [ARCH. NEUROL. & PSYCHIAT.]

REWARD AS AN AID FOR THE CHILD IN TRAINING. F. HAMBURGER, Med. Klin. **34**:674 (May 20) 1938.

One of the best forms of reward is the friendliness and good will of the parent. Reward in the form of food, especially a delicacy, may be of value in training for eating habits. Reward in the form of gifts or excursions should be utilized infrequently, as frequent use will destroy their effectiveness and will tend to instill a sense of materialism and greed. Once a reward is promised it must be forthcoming.

Training by prohibition is attended by an unpleasant feeling; training by command or request and regard, by a pleasant feeling. The former type of training should be attained by about 18 months; the latter is usually not attained until the end of the third or fourth year. Training for obedience by reward can be begun at the end of the first year by teaching the significance of "please." In uttering a prohibition the tone of voice must be firm; in uttering a command or a request it must be pleasant. The child's mood is important. If the mood is disagreeable, a command or a request had better be omitted until the mood is more favorable, as a child in an unfavorable mood is unable to comply. Force in eliciting compliance is inadvisable, at least until the end of the third or fourth year.

SIEMSEN, Chicago.

BRINGING UP AND TEACHING OF CHILDREN IN INSTITUTIONS FOR THE SICK. M. SKOKOWSKA RUDOLFOWA, Zycie Mlodych **7**:132 (May) 1938.

At the conferences of the boards of many institutions in Poland an important question came up as to why institutions for the sick could not become teaching institutions. For example, a child who is sick with tuberculosis and needs institutional care also needs to be educated. All these institutions should have teaching facilities. The motto should be: "A hospital is a home, and the patient is the guest."

KRUPINSKI, Chicago.

PROBLEMS IN CHILD GUIDANCE FROM THE POINT OF VIEW OF A PEDIATRICIAN. B. LEICHTENTRITT, Acta pædiat. **23**:93, 1938.

Addressing himself to the physician as the "guide of those who guide the young," Leichtentritt offers mature and mellow advice on bringing up children. Unless it is the reader's first excursion into this kind of literature, he will discover little that is novel; he will, however, find acceptance of certain theories derived from modern psychiatric thought combined in a hard-headed but kind-hearted way with principles based on nontechnical human experience, sometimes known as common sense. The topic loses something from oversimplification and through the curtailment necessary to compress it into 25 pages: Notably, some will not agree that the end and highest attainment of education is the development of *Anpassungsfähigkeit* (adaptability) in its disciples. MCCUNE, New York.

Diseases of the Genitourinary Tract

ENURESIS AND OTHER FACTORS IN NORMAL AND IN PSYCHOTIC PERSONS: A COMPARATIVE STUDY OF INCIDENCE AND INTERCORRELATIONS. J. J. MICHAELS and S. E. GOODMAN, Bull. Neurol. Inst. New York **7**:699 (Sept.) 1938.

The incidence of neurotic symptoms (thumb sucking, nail biting, impediments in speech, poor sleeping habits and fears) was found significantly lower in 224 psychotic patients than in 475 so-called normal children. "The low incidence of nose picking, moodiness, easy fatigability, delinquency, resentments and vasomotor disturbances in the psychotic patients was striking." The psychotic patients showed a higher incidence of temper tantrums, however.

This study was purely statistical. BEVERLY, Chicago.

URINARY INFECTIONS IN INFANCY AND CHILDHOOD: DIAGNOSIS AND TREATMENT. H. F. HELMHOLZ, J. A. M. A. **111**:1719 (Nov. 5) 1938.

The diagnosis of urinary infection in an infant or a child involves not only finding fever and pyuria but also absence of renal damage, usually produced by stasis. The offending organism should be investigated as well, which with evidence of kidney function determines the preferred method of treatment. With advance in therapy infection may be cleared and obstruction still exist; this should be checked by urographic examination, even in cases of cure.

Factors to be considered in choice of treatment are ease of administration, toxicity, action on various bacteria and p_H of the urine.

At present sulfanilamide and mandelic acid are the drugs of choice, the former in a wide range of infection, the latter particularly in those due to Streptococcus faecalis and some other types. The procedure used in each case is described.

HEERSMA, Kalamazoo, Mich.

WILMS' TUMORS. G. W. REAGAN, South. M. J. **31**:1129 (Nov.) 1938.

Reagan states that nearly every abdominal tumor occurring in infancy or childhood is an embryonal tumor of the kidney.

Early diagnosis, as with other malignant tumors, is of utmost importance. It can often be made by urologic study of a patient who has a long-continued, low grade fever, not otherwise explained, with leukocytosis, digestive disturbances and loss of weight.

Wilms' tumor is highly radiosensitive. In all cases it should be adequately treated with irradiation before operation. The best time to operate is three to six weeks after proper irradiation. SCHLUTZ, Chicago.

CONGENITAL VALVES OF THE POSTERIOR URETHRA. E. S. MOSS and J. R. SCHENKEN, South. M. J. **31**:1134 (Nov.) 1938.

Moss and Schenken report a case of congenital valves of the posterior portion of the urethra, associated with spina bifida occulta, a retrotrigonal pouch and a diverticulum of the bladder, with special reference to the postmortem observations. The association of spina bifida occulta with the urethral anomaly differentiates this case from others on record in the literature.

Congenital valves of the urethra must be searched for in every male child with prolonged infection of the urinary tract if the condition is to become a definite clinical entity rather than to remain a postmortem curiosity.

SCHLUTZ, Chicago.

EXPECTANCY OF LIFE AFTER URETERAL TRANSPLANTATION. H. WADE, Edinburgh M. J. **46**:61 (Feb.) 1939.

Although Wade deals with malignant growths, obstetric injuries, burns and diseases of various types, he reports favorable results from transplanting the

ureters into the pelvic colon in patients who did not offer forlorn hopes at the time of operation. The most promising conditions are malformations of congenital or accidental origin. The histories of some of these had been known since childhood. The transplantations permit the patients to live useful and healthy lives. The tables furnished show a high percentage of recoveries in the patients with nonmalignant conditions.

NEFF, Kansas City, Mo.

FURTHER OBSERVATIONS ON THE HORMONE TREATMENT OF IMPERFECT DESCENT OF THE TESTIS. A. W. SPENCE and E. F. SCOWEN, Lancet **2**:983 (Oct. 29) 1938.

The treatment of retained testes with a gonadotropic extract from the urine of pregnant women should be employed in those cases in which retention does not appear to be due to anatomic abnormality. The dose in most cases should not be less than 500 rat units, given intramuscularly twice a week. The optimum age for treatment is between 10 and 14 years. Testes which are situated in the inguinal canal, which are movable but which cannot be manipulated into the scrotum, will probably respond to this therapy (usually within six or nine months). In patients in whom there is no improvement within six months there is probably an anatomic abnormality. The latter is more apt to be present in the case of unilateral than in that of bilateral retention. In patients of suitable age there are no serious contraindications to treatment.

LANGMANN, New York.

GRAVER TYPES OF COLON BACILLUS INFECTION IN THE INFANT'S URINARY TRACT. L. RIBADEAU-DUMAS and J. CHABRUN, Arch. de méd. d. enf. **41**:785 (Dec.) 1938.

Although most invasions of the urinary system by the colon bacillus are essentially benign and are readily cured, occasionally cases of severe infection are encountered. A prime factor in these instances is congenital malformation, such as hydronephrosis, stenosis of the ureter or faulty development of the bladder. To determine such organic defects, roentgenographic study of the urinary tract is mandatory.

Another feature of these infections is the presence of special strains of the colon bacillus; in some cases there are associated micro-organisms. The authors recognize three types in their clinical observations, the first being a so-called nervous form in which catatonia is noted, the second a pseudosurgical variety with thrombosis of the renal vein and hypertrophy of the corresponding kidney, and the third a symbiosis leading to multiple lesions, such as pyelonephritis, staphylococcic pulmonary abscess and pneumococcic mastoiditis.

Numerous case histories are quoted to illustrate these three categories and to demonstrate the polymorphism of infantile infection with colon bacilli.

AMESSE, Denver.

A COMPARISON OF ORGANIC ACIDS AND SULFANILAMIDE AS URINARY ANTISEPTICS. H. F. HELMHOLZ, Acta pædiat. **23**:1, 1938.

The originator of the first really effective treatment of infections of the urinary tract summarizes his experimental and clinical experience in the following words:

"The introduction of organic acids and sulfanilamide has greatly improved the chances of curing urinary infections. Betaoxybutyric acid and mandelic acid are dependent for their action on a concentration greater than 0.5 per cent and a p_H of the urine less than 5.5, so that treatment is not likely to be successful unless the function of the kidney is normal or nearly so. The inability to reduce the p_H of the urine of patients with Proteus infections makes organic acid therapy almost useless in the treatment of such infections. The action of such organic acids on Streptococcus faecalis, however, makes them the antiseptics of choice for this type of infection.

"Sulfanilamide, because of its ease of administration and tolerance by the stomach, is the preferable drug in the average case. It is the drug of choice during the acute stage of the disease. Acting best in an alkaline urine, sulfanilamide is extremely useful in treating infections of the Proteus group. It has also proved its usefulness in the treatment of patients with reduced renal function. Its striking ineffectiveness in the treatment of Streptococcus faecalis infections, however, is a definite handicap.

"These drugs, one group acting only in an acid and the other best in an alkaline medium, supplement each other, and they should be used in the treatment of urinary infections according to the type or types of organisms causing them."

The bibliography is brief but comprehensive. McCUNE, New York.

Diseases of the Ductless Glands; Endocrinology

CHRONIC IDIOPATHIC PARATHYROID TETANY. A. CANTAROW, H. L. STEWART and D. R. MORGAN, Endocrinology **24**:556 (April) 1939.

This is a report of a carefully studied case of severe chronic hypoparathyroidism. The patient was a white child who was under observation from the age of 6 years until her death at the age of 12 years. Symptoms of tetany appeared first at the age of 3½ years; these did not respond to vitamin D therapy but were effectively controlled by large doses of parathyroid extract and a high calcium, relatively low phosphorus intake over a period of five and a half years. This regimen became ineffective on two occasions, when the only change consisted in an increase in the intake of phosphorus (and calcium) and vitamin D, and became effective again when the latter were omitted. The significance of this phenomenon is discussed. Death was due apparently to the development of a peculiar hemorrhagic state, with extensive hemorrhages throughout the body. The exact nature and pathogenesis of this state could not be determined; it may have been dependent on a deficiency in prothrombin.

No parathyroid tissue could be found at autopsy. Aside from the hemorrhagic manifestations, the only other significant findings were mild chronic hepatitis, mild nephrosis, bronchopneumonia and trophic changes in the hair, nails and teeth.

JACOBSEN, Buffalo.

A CASE OF PITUITARY DWARFISM TREATED WITH ANTUITRIN-G. J. A. BUCHANAN and H. A. BALLWEG, Endocrinology **24**:565 (April) 1939.

The case reported is that of an 18 year old girl with dwarfism, infantilism and severe headaches resulting from pituitary insufficiency, due to external pressure on the hypophysis and hypothalamic structures by a slowly growing tumor mass. Surgical treatment and irradiation were refused. An extract of the anterior lobe of the pituitary gland said to contain the growth hormone (antuitrin G) was given to determine its efficacy. As there had been no change in height, weight or physical appearance for seven years, there seemed to be a definite response to the growth properties of this medication, shown by the increase in height of 3 cm., the increase in weight of 8 Kg., the appearance of axillary hair, the establishment of catamenia and the enlargement of the breasts. The decrease for some time in the severity and frequency of headaches, vomiting, nausea, dizziness and orbital pain was undoubtedly due to variation in the size of the tumefaction and was not directly related to the therapy. JACOBSEN, Buffalo.

THE THYMUS. A. G. MITCHELL and J. WARKANY, J. A. M. A. **112**:283 (Jan. 28) 1939.

One of the most rare causes of cyanosis, dyspnea, stridor or dysphagia may be enlargement of the thymus gland. When this organ is proved to be at fault, roentgenologic treatments are indicated to reduce its size. There seems to be no

relation between this condition and the so-called status thymicolymphaticus. As to the endocrine nature of the gland, what little information is at hand, is not of practical value. HEERSMA, Kalamazoo, Mich.

RADIOLOGY'S RESPONSIBILITY IN THE DIAGNOSIS AND TREATMENT OF THYMIC HYPERPLASIA. C. K. HASLEY, J. A. M. A. **112**:285 (Jan. 28) 1939.

Hasley was unable to correlate apparent enlargement on roentgen films with the size of the thymus at autopsy or with the symptoms. He knew of no standard to determine enlargement and did not feel that treatment was indicated merely because of enlargement on roentgenograms. HEERSMA, Kalamazoo, Mich.

DIETETIC AND INSULIN MANAGEMENT OF THE JUVENILE DIABETIC. P. H. HERRON, New Orleans M. & S. J. **91**:423 (Feb.) 1939.

In managing diabetes in children one must take into consideration the growth and education of the child and the severity, instability and progression of the disease. The ideal attainment is to produce a normal blood sugar throughout the twenty-four hours without shock or glycosuria—to produce normal growth and allow a happy existence. Individualization of dosage is necessary and is based on frequent determinations of the blood sugar and urinalyses. Hospitalization is recommended for new patients until the proper routine is established. Juvenile patients respond to protamine zinc insulin well.

A diabetic child cannot have a normal diet without insulin, and a diabetic child will not adhere to an inadequate diet. Most children do best on a high carbohydrate–low fat diet, because of a better metabolic balance; they show less tendency to go from hypoglycemia to hyperglycemia, a lowering of the insulin requirements in many cases, less tendency toward development of premature arteriosclerosis, better adherence to the diet, an increase in carbohydrate tolerance and an increase in weight, strength and energy. A weighed diet is urged for the best control of the disease. Proper control allows normal growth and development and a happy existence. BERKLEY, Los Angeles.

EXOPHTHALMIC GOITRE IN CHILDREN. F. R. B. ATKINSON, Brit. J. Child. Dis. **35**: 165 (July-Sept.); 267 (Oct.-Dec.) 1938.

This report is based on an analysis of 208 cases of exophthalmic goiter in children which the author has been able to collect from the literature.

The cases are analyzed for the occurrence of the four chief characteristic findings, viz., tachycardia, enlargement of the thyroid gland, exophthalmos and tremor.

No new light is thrown on possible causes.

The disease has been reported in mother and child or in brothers and sisters numerous times.

The incidence in females is about four times that in males (as in adults). It is rare in children less than 3 years of age.

To the characteristic findings Bram adds another, viz., the ability to take at least 5 grains (0.31 Gm.) of quinine sulfate thrice daily without showing sgns of cinchonism.

The statement is made that the prognosis for children with this disease seems better than that for adults. LANGMANN, New York.

EXOPHTHALMIC GOITER IN CHILDREN. D. D. SOKOLOW, Vrach. delo **20**:455, 1938.

Sokolow presents a complete review of the clinical features and causes of exophthalmic goiter in children, with a report of 2 cases.

Of 18 children with severe forms of this disease whom he observed, 16 were girls and only 2 were boys. Of the 361 with light or moderate forms, 303 were girls and 58 were boys.

Enlargement of the thyroid was almost constant, occurring in all of the 18 children with the severe forms and in 351 of those with the lighter forms. Tachycardia was also observed in all those with severe, and in 55 per cent of those with light and moderate, forms. Exophthalmos occurred in 66 per cent of the patients. Increased nervous excitability was one of the earliest manifestations. Increased growth was noted in about 77 per cent, as was hypoplasia of the sex glands and delay in sexual development. Lymphocytosis occurred in a number, also hyperhidrosis and diarrhea.

The basal metabolic rate is considered to be of secondary value as an index, as low rates were frequently obtained in cases of severe disease and vice versa. The blood sugar is not as high in children with this disease as it is in adults.

Sokolow has observed that mild forms of the disease in children are frequently transformed into severe forms in adults. This, he states, is contrary to the general belief that symptoms of hyperthyroidism in girls diminish with the onset of menstruation. On the whole, exophthalmic goiter runs a lighter course in children than in adults. Spontaneous recovery may occur.

It is pointed out that exophthalmic goiter is a disease not of the thyroid gland alone but of the entire organism.

Sokolow's conclusions follow:

1. In children clinical exophthalmic goiter is characterized by the same basic symptoms as in adults.

2. Increased growth and acceleration of the ossification processes are characteristic of the disease in childhood.

3. Three grades of severity of the disease may be distinguished: light, moderate, severe. Patients with the last form invariably require hospitalization, while patients with the light and moderate grades may be ambulatory.

4. The disease, though occurring most commonly in preadolescent girls, may attack children of all ages.

5. In treatment the same methods are used for children as for adults, namely, organotherapy, physical therapy and surgical excision. BODER, Los Angeles.

A CASE OF PINEAL TUMOR. K. SASAKI and Y. ISHIMARU, Acta pædiat. japon. **44**:1771 (Nov.) 1938.

A case of pineal tumor in a boy 11 years old is reported. No abnormalities either in general physical or in sexual development were noted during life. The patient complained of difficulty in hearing several years before death, especially during the winter seasons. For several months prior to death he had severe epileptiform convulsions. Then severe headache, diplopia and increased difficulty in hearing developed, accompanied by vomiting. After hospitalization the patient became lethargic, and spasticity of the neck developed. The spinal fluid was under increased pressure, and slight papilledema was noted in the ocular fundi. Autopsy revealed a tumor in the pineal gland. Twenty-eight cases of this type of neoplasm reported in the Japanese literature are reviewed. K. KATO, Chicago.

NEUROBLASTOMA OF THE LEFT ADRENAL WITH INTRATHORACIC METASTASES. J. REURINK, Acta pædiat. **23**:78, 1938.

A healthy 15 month old baby suddenly exhibited difficulty in walking; on the following day she cried because of pain in the right thigh, then because of pain in the left, and refused to sit erect. Twelve days later it was recognized that she had a high transverse lesion of the spinal cord. Vasomotor and secretory disturbances were present on the right side of the body; the left eyelid showed ptosis. A diagnosis of disseminated encephalomyelitis was entertained until the development of signs of a mediastinal mass made it seem more probable that the lesion of the cord was of metastatic origin.

Autopsy revealed a small neuroblastoma of the left adrenal together with a much larger mass of similar structure in the posterior part of the mediastinum. The paraplegia was found to be due to compression of the spinal cord and to ischemic necrosis resulting from occlusion of a vessel. Examination of the left orbit was not permitted, but it was warrantably assumed that the ptosis had been due to a local metastasis.

The author discusses briefly the clinical and histologic classification of the ganglioneuroma-neuroblastoma group of new growth. McCUNE, New York.

Diseases of the Muscles, Bones, Joints and Lymph Glands

PSEUDOHYPERTROPHIC MUSCULAR DYSTROPHY. L. SCHEMAN, P. LEWIN and S. SOSKIN, J. A. M. A. **111**:2265 (Dec. 17) 1938.

Scheman, Lewin and Soskin review here the many types of treatment for myodystrophic patients. They have checked the principles underlying pancreatin ferment therapy by examinations of the stool, urine and duodenal contents. There was no evidence from this work on 5 patients that the metabolism of nitrogen is impaired, that the dextrose tolerance is abnormal or that pancreatin extract has any effect on the excretion of creatine or creatinine.

Clinically, improvement followed the regularity instituted with this study, regardless of therapy. The authors feel that the future prospects for successful treatment lie in further investigation of the muscle pigment or of the metabolism of myoglobin. HEERSMA, Kalamazoo, Mich.

QUININE IN MYOTONIA CONGENITA. R. B. LONERGAN and H. PASKIND, J. A. M. A. **111**:2292 (Dec. 17) 1938.

The literature dealing with the use of quinine in the treatment for myotonia congenita is reviewed and a case presented of a 14 year old boy with marked myotonia in whom relief of symptoms was maintained with 15 grains (1 Gm.) of quinine daily. HEERSMA, Kalamazoo, Mich.

HEREDITARY ARTHRODYSPLASIA ASSOCIATED WITH DYSTROPHY OF THE NAILS. J. W. SEVER, New England J. Med. **219**:87 (July 21) 1938.

The condition is purely inherited and congenital and is apparently due to some defect in the closing or fusing of the ectodermal and mesodermal layers of the embryo. The degrees of the deformity vary in different subjects; one may show the skeletal defects; another, simply the nail defects; or the two kinds of defects may be combined, as in the case reported. Treatment is of avail only in youth, and then it is directed only toward the dislocation of the patellas.

GENGENBACH, Denver.

AN INVESTIGATION OF THE SOURCE OF STAPHYLOCOCCAL INFECTION IN ACUTE OSTEOMYELITIS. S. WILLIAMS and C. TIMMINS, M. J. Australia **2**:687 (Oct. 22) 1938.

Because of fluctuations from year to year in the number of patients with acute osteomyelitis treated at the Children's Hospital, Melbourne, Australia, the authors suggest that the relative frequency of the disease might in some way be influenced by differences in the types of staphylococci prevalent in the child community at different periods. It is well known that Staphylococcus aureus is a not uncommon inhabitant of the upper respiratory tract. If certain strains producing such subclinical infections were more likely than others to settle in a damaged epiphysial junction, a possible explanation of these periodical fluctuations would be available. An attempt to detect individual differences between strains of Staphylococcus aureus was made on the basis of their reactions to a series of phages. The method

is described and the difficulties thereof discussed. The types of staphylococci obtained from the bone lesion and the nose and throat in 19 cases are listed, but because of the difficulties in the interpretation of results the authors make only a general conclusion as follows: "In children suffering from osteomyelitis a proportion harbours the same type of staphylococcus in the nose and throat as is present in the bony lesion." GONCE, Madison, Wis.

SOME ASPECTS OF THE PATHOLOGY OF BONE TUMOURS OF INTEREST TO RADIOLOGISTS. R. A. WILLIS, M. J. Australia **2**:717 (Oct. 29) 1938.

In a series of 500 consecutive autopsies on persons who died of malignant disease Willis found 69 metastatic and only 8 primary tumors of bone. He stresses the need for accurate diagnosis and thorough study in cases of tumor of bone considered primary, for in many such cases the tumor has proved at postmortem examination to be secondary to visceral carcinoma. The pathologic pictures and the differential diagnoses of metastatic carcinoma, multiple myeloma and osteogenic carcinoma are discussed. Because of the frequency with which metastatic carcinoma or neuroblastoma is encountered at autopsy in cases in which a tumor has been classified antemortem as Ewing's tumor the author doubts that there is any such pathologic entity as Ewing's tumor. GONCE, Madison, Wis.

MUSCULAR ATROPHIES AND DYSTROPHIES IN CHILDHOOD. R. J. TAYLOR, M. J. Australia **2**:889 (Nov. 26) 1938.

1. Infantile muscular atrophy.
   - (*a*) Werdnig-Hoffmann type. Paralysis of the proximal muscles appears during the first year with steady progression. Death results from paralysis of the respiratory muscles. There are no sensory disturbances.
   - (*b*) Oppenheim's disease. This is characterized by extreme weakness of all muscles, usually noticed at birth. There are no sensory changes.

2. Neuritic type. Atrophy usually begins in the peroneal group, affecting first the anterior tibial muscle. Later it attacks the intrinsic muscles of the hand and forearm, resulting in clawhand. Sensory changes are usually present, causing pain, hyperesthesia, paresthesia and like conditions. The disease is hereditary and affects both sexes.

3. Muscular dystrophies.
   - (*a*) Pseudohypertrophic type. This affects almost entirely males, but may be transmitted by healthy females. It usually begins at about the fourth year of age, producing the characteristic pseudohypertrophy of the calf muscles.
   - (*b*) Juvenile type. This commences in early adolescence and affects first the scapulas, causing difficulty in raising the arms above the head. The muscles of the face and neck are unaffected. The shoulder girdle is markedly atrophied. It then spreads to the upper part of the arm but leaves the forearm unaffected. Later the pelvic girdle and thigh become involved. The muscles of the leg remain normal.
   - (*c*) Facioscapulohumeral type. This type is similar to the foregoing type, but the muscles of the face are also affected.
   - (*d*) Distal type. This type is rare. Atrophy commences in the hands and feet and slowly extends up the extremities.

4. Myotonia atrophica. This is a hereditary and familial disease causing atrophy of the facial muscles and of the muscles of the forearm and hand. One of the characteristic symptoms is inability to relax the grip quickly.

In the biochemistry of the myopathies the following conditions obtain: (1) hypoglycemia, (2) disturbance of sugar tolerance, (3) hypocholesteremia, (4) creatinuria with disturbances of creatine tolerance, (5) diminution of urinary creatinine and (6) normal blood creatine content.

Taylor has never seen treatment of the dystrophies with aminoacetic acid do any good. He believes that those having a hereditary and familial tendency should be treated along eugenic lines. He believes that the trophic disturbances associated with the dystrophies may be treated by chemical means and has used physostigmine and its derivatives with good results. TENNEY, Madison, Wis.

OUTLAWING OF EMERGENCY OPERATIONS IN THE TREATMENT OF ACUTE OSTEOMYELITIS IN CHILDREN. J. LEVEUF, Bull. Soc. de pédiat. de Paris **36**:135 (March) 1938.

In 21 of 29 cases of acute osteomyelitis blood cultures yielded pure growths of Staphylococcus aureus. In 7 cases the illness terminated in death. The period of invasion, with fever and toxemia, lasted from fifteen to twenty-five days. The disappearance of organisms from the blood stream coincided with the return of the temperature to normal. Fulminating septicemic osteomyelitis occurs, but repeated positive cultures while the patient improves indicate simply that bacteria are being eliminated from the site of infection in the bone and are carried by the blood stream to the kidneys from which they pass into the urine. Positive blood cultures, therefore, do not necessarily indicate a poor prognosis. For the past three years no trephining has been done for acute osteomyelitis, in order to avoid any interference with the natural barrier which tends to circumscribe the infection. The involved limb is put at rest in a plaster cast and observed. Only when a definite collection of pus has developed is an incision made to evacuate it. Sequestrums have been fewer, smaller and more easily removed when removal was necessary, and the results have been better, with this method of treatment.

BENJAMIN, Montreal, Canada.

TREATMENT OF ACUTE OSTEOMYELITIS. E. SORREL, Bull. Soc. de pédiat. de Paris **36**:221 (April) 1938.

Acute osteomyelitis is a suppurative lesion, and the old adage *ubi pus, ubi evacua* should be followed in the treatment of this condition. Discussion centers about the time and the type of intervention. The results aimed at are subsidence of the acute process and avoidance of a chronic lesion. Three fourths of staphylococcic infections of bone are more or less self limited; a second group, the pyemic variety, urgently require surgical intervention, while the fulminating staphylococcic septicemia without early localization does not present indications for surgical intervention. When only a subperiosteal abscess is present, simple incision is performed; when a central abscess is present, the bone is trephined, and when the periosteum has been stripped away from the bone along its entire circumference or when necrosis is present, resection of the diaphysis is in order. Immobilization of the limb in a plaster cast, which is disturbed as infrequently as possible, completes the treatment. Intravenous injections of antiserum to produce marked reactions were used in testing patients with severe lesions, with presumably some good effect, but anatoxin is not credited with any beneficial results. Of 83 patients with suppurative osteomyelitis, 13 were treated by means of simple incision; 29, by incision and trephining of the bone, and 41 by diaphysial resection. When in doubt, Sorrel leans toward resection of the diaphysis.

BENJAMIN, Montreal, Canada.

MYATONIA CONGENITA IN IDENTICAL TWINS. K. THUMS, Ztschr. f. d. ges. Neurol. u. Psychiat. **162**:233 (March) 1938.

Thums reports 2 cases of myatonia congenita in identical twins. The parents were related. The illness began in both twins at the age of 4 or 5 months. They

did not move as much as normal children and at the age of 2 years could neither sit nor stand. The knee jerks were absent. The mental development was normal. Weakness and atonia were more marked in the legs. The proximal muscles were relatively spared. The respiratory muscles were finally involved. No fibrillations were noted. There were no circumscribed muscular atrophies. Both twins died of bronchopneumonia, two years apart. The presence of myatonia in identical twins is in favor of the importance of a genetic factor in the causation of this disease. SAVITSKY, New York. [ARCH. NEUROL. & PSYCHIAT.]

HEMANGIOMA OF THE VERTEBRAL COLUMN. I. S. ROSENTSWEIG, Sovet. psikhonevrol. **14**:47, 1938.

According to Rosentsweig, hemangioma of the vertebral column is a benign vascular neoplasm developing frequently on the basis of a congenital anomaly of the vascular system. In the great majority of cases the tumor is observed accidentally at necropsy. Hemangioma only rarely gives rise to clinical manifestations. The growth is capable, however, of producing a clinical picture of compression of the spinal cord. Of the 5 patients observed by the author, 4 presented symptoms of compression of the spinal cord. The diagnosis of hemangioma of the vertebral column is possible only on the basis of roentgenologic examination. A hemangioma causing compression of the cord may be treated by operative intervention or by roentgen irradiation. The former has a higher mortality because of profuse bleeding. Roentgen irradiation has been widely used in the treatment of this condition, with gratifying results. The author reports cure in 3 of his 4 patients so treated and improvement in the fourth.

EDITOR'S ABSTRACT. [ARCH. NEUROL. & PSYCHIAT.]

Diseases of the Eye

SOME ASPECTS OF STRABISMUS. E. F. BIRKENSTOCK, South African M. J. **12**: 833 (Nov. 26) 1938.

Birkenstock reviews the chief causes of strabismus. He stresses the need for accurate diagnosis and for treatment with unbreakable lenses at the age of 1 year. When the eyes are not satisfactorily corrected with glasses, or when the infant cannot become accustomed to glasses, the fixing eye should be covered in order to stimulate the affected eye. If lenses and patching fail to abolish the squint and correct the visual axis, the correction should be accomplished by tenotomy and advance of the muscles at fault. This procedure should not be done later than the fifth year of age, because the power of fusion of the separate but identical retinal images is apparently lost after the age of 6 years. Prisms and orthoptic treatments should be used to stimulate fusion and binocular single vision.

GONCE, Madison, Wis.

TAY-SACHS DISEASE. R. DIAZ, Bol. Soc. cubana de pediat. **10**:652 (Nov.) 1938.

Diaz presents 2 cases of Tay-Sachs disease. One patient was a 19 and the other a 15 month old infant. The ocular changes and the differential diagnosis are given. SCHLUTZ, Chicago.

FAMILIAL GLIOMA. J. KOLACNY, Bratisl. lekár. listy **16**:312 (Nov.) 1936.

Glioma originates in the ectodermal layer of the retina during intrauterine gestation, thereby raising the question of heredity and familial tendency. Sattler divides glioma into the very rare hereditary glioma and the more frequent glioma in apparently healthy siblings. The author cites 6 siblings, of whom 3 had glioma; of these, 2 died, owing to resistance to enucleation. The points in the summary are: gliomatous children die before puberty; in 85 per cent of cases glioma is unilateral; there may be a mutation form or a recessive mendelian

factor; sterilization should be considered for persons afflicted with glioma; an increased incidence is noted in Jews; inbreeding may be a factor; a similarity is suggested here to the factor of heredity in the incidence of malignant tumors. Kolacny stresses the importance of educational propaganda for early enucleation.

STULIK, Chicago.

CHOLESTERINOSIS BULBI. P. M. GEORGARIOU, Arch. f. Ophth. **139**:32 (Aug.) 1938.

The left eye of a 14 year old girl had sustained an apparently blunt injury ten years previously. At the time of the clinical examination it was inflamed, soft and blind; the iris was atrophic and hyperemic, and the lens was cataractous. The lower half of the anterior chamber was filled with a solid-looking white mass, whereas in the upper half innumerable needle-shaped crystals were floating about. The anterior chamber was emptied by keratome incision; the white mass and the floating crystals proved to be cholesterol. One day after paracentesis the anterior chamber was again found to be partly filled with crystals. The author calls this rare condition cholesterinosis bulbi. He considers it to be essentially different from the various forms of lipoidosis bulbi and speculates as to its pathogenesis.

KRONFELD, Peiping, China. [ARCH. OPHTH.]

FATE OF PATIENTS SUFFERING FROM PHLYCTENULAR DISEASE, WITH PARTICULAR REFERENCE TO TUBERCULOSIS. A. AJO, Acta ophth., 1938, supp. 15, p. 1.

This monograph first gives a historical review of ideas which have been held in regard to the causes and pathogenesis of phlyctenular disease. It then deals with the question of the prognosis of ocular phlyctenulosis, with particular regard to the later development of tuberculosis.

In the university clinic for persons with ocular diseases at Helsingfors, Finland, there were 449 patients with phlyctenular disease between 1912 and 1927. Ajo succeeded in tracing 367 of these patients. He found that 55 had died. Tuberculosis was the cause of death of 35, and in 4 more it was the probable cause, making the mortality rate for tuberculosis 10.62 per cent. This is about double the mortality rate for tuberculosis in persons of the same age group in the general population of Finland.

Of the former patients still living, 100 were thoroughly examined; 50 were found free from disease. Of the remaining 50 patients, 39 showed tuberculous changes, 5 showed changes which were probably tuberculous, and 6 showed other pathologic changes. Pulmonary tuberculosis was found in 7 patients. Ajo concludes that it may not be held that patients with phlyctenular disease will be spared later severe tuberculosis.

PERKINS, New York. [ARCH. OPHTH.]

Skin Diseases; Allergy

CONGENITAL XANTHOMA TUBEROSUM. H. CHARACHE, Am. J. Cancer **31**:563 (Dec.) 1937.

Charache reports a case of xanthoma tuberosum in a baby. The lesion developed at a site of trauma and in the absence of cholesteremia. The histologic sections showed an abundance of giant cells but no xanthoma cells.

FOERSTER, Milwaukee. [ARCH. DERMAT. & SYPH.]

CONTACT AND ENVIRONMENTAL ALLERGENS AS A CAUSE OF ECZEMA IN INFANTS AND CHILDREN. E. D. OSBORNE and H. L. WALKER, Arch. Dermat. & Syph. **38**:511 (Oct.) 1938.

Experimental observations and a review of the literature on eczema in infants and children led to the following conclusions and comments:

In dealing with eczema in infants and children an investigation of contact and environmental allergens yields a high percentage of satisfactory results.

There is no experimental evidence that a person inherits any specific epidermal sensitivity. He inherits "ease of sensitization" or "susceptibility to sensitization."

The widespread use of ammoniated mercury in the prophylaxis of impetigo contagiosa in the newborn is an imporant factor in producing eczema in infants and in widening the base of their allergy.

Routine scratch and intradermal tests are inadequate, unreliable and misleading. Routine patch tests are not usually satisfactory. Actual clinical trial is more important. Patch tests with protein substances generally produce negative results in infants and children. As widely used, they do not conform to the first rule of patch testing, namely, that clinical conditions must be duplicated.

In an etiologic study of eczema of infants and children the first attack should be by elimination of contact and environmental allergens. With this method the authors succeeded in obtaining the following results: cures in 50 per cent of the patients, improvement in 35 per cent and no change in 15 per cent. In the "improved" group, the authors believe there were multiple sensitivities not only to contact and environmental allergens but to food atopens and possibly to metabolic products. From their experience they do not believe that food atopens are of importance in more than 15 to 20 per cent of infants and children with eczema. They believe that transepidermal absorption of water-soluble protein allergens through both inflamed and noninflamed skin explains many of the clinical facts observed in patients sensitized to these allergens.

A painstaking investigation of the history, a highly developed detective instinct and infinite attention to detail are more important than routine tests of any kind in determining the cause of eczema in infants and children.

JACKSON, Iowa City.

ALLERGY IN INFANTS: SIGNIFICANCE OF FIRST ALLERGIC MANIFESTATIONS. N. W. CLEIN, Northwest Med. **38**:9 (Jan.) 1939.

A series of 100 allergic and 100 nonallergic infants were studied from birth to the age of 4 or 5 years. The feedings, examinations and observations were uniform in all cases.

Of the allergic infants, 71 per cent had allergic parents; of the nonallergic, 12 per cent.

Of the allergic infants, 78 per cent exhibited some allergic symptoms before the fourth month of age, 91 per cent by the end of the first year and 100 per cent by the end of the second year of age, as follows: rash (eczema), occurring chiefly on the face (85 cases); vomiting (pylorospasm) (24 cases); colic (abdominal pain, gas or diarrhea) (16 cases). Frequently one or more of these symptoms were present at the same time.

Egg yolk should not be added to the diet of allergic infants too early, as many are sensitized through the mothers' milk or inherit the sensitivity.

Often taking of a family history, study of the present allergy, elimination and testing are necessary for a proper solution. ROBERTSON, Omaha.

BAYER 205 IN THE TREATMENT OF LUPUS ERYTHEMATOSUS. B. CHAJES, Lancet **2**:1288 (Dec. 3) 1938.

Germanin (Bayer 205) was used in the treatment of 13 patients with lupus erythematosus; 9 were cured, and the remaining 4 showed considerable improvement. Recurrences after the first course of treatment were observed in 6 of the patients, but a second course usually effected a cure. The drug was injected intravenously in a 10 per cent solution. The injections were given very slowly and at an interval of five to seven days. Chajes was induced to use the drug in this disease because of the favorable results obtained with it in pemphigus. The formula of the drug is not given. LANGMANN, New York.

RAPID DEATH FROM ECZEMA IN INFANCY: ROLE OF THE NEUROVEGETATIVE SYSTEM. R. A. MARQUÉZY, ALAJOUANINE, LADET and HORNET, Bull. Soc. de pédiat. de Paris **36**:165 (March) 1938.

A breast-fed, well nourished boy 4½ months old was admitted to the hospital because of a generalized scarlatiniform eruption which was diagnosed as acute eczema. He had high fever and convulsions which were due apparently to tetany. After the first forty-eight hours he improved temporarily but soon became worse and died on the eighth day after admission. Necropsy revealed vasodilatation throughout the viscera, including the nervous system, in addition to intra-abdominal lymphoid hyperplasia. The findings resembled those encountered in anaphylactic shock, which is believed to be a factor in the causation of violent fatal illness occurring in association with eczema in infants.

BENJAMIN, Montreal, Canada.

A CASE OF SCLEREDEMA. HALLÉ, PICHON and CHAREIRE, Bull. Soc. de pédiat. de Paris **36**:181 (April) 1938.

A 9 year old girl presented signs of scleredema a month after she recovered from measles. The skin showed edema and did not pit on pressure, and there was loss of the normal elasticity. There were no scars, no sclerosis and no violet discoloration such as is observed about plaques of scleroderma. There was a rash about the pelvis. Her heart beat was of the gallop rhythm type. The electrocardiogram was normal. This cutaneous condition usually clears up in a few months but may be followed by scleroderma. Small doses of thyroid extract were prescribed.

BENJAMIN, Montreal, Canada.

ACUTE ACCIDENTS IN ECZEMATOUS INFANTS. M. LESNÉ, Bull. Soc. de pédiat. de Paris **36**:191 (April) 1938.

The rapid or sudden death which occurs not infrequently in infants with eczema is believed to be in the nature of anaphylactic shock.

BENJAMIN, Montreal, Canada.

CONGENITAL NEVI AND DERMATOLYSIS (ATYPICAL RECKLINGHAUSEN'S DISEASE). G. DREYFUS-SEE and S. WIRZ, Bull. Soc. de pédiat. de Paris **36**:231 (April) 1938.

A boy almost 3 years old had an enormous hairy pigmented nevus which extended over most of the right half of the scalp. There were also numerous small areas of pigmentation over the body, some of which were covered with hair. No other abnormalities were found.

BENJAMIN, Montreal, Canada.

DERMATITIS FROM CONTACT WITH GARLIC. DARIO SEPULVEDA, Arch. Hosp. Niños Roberto del Rio **8**:64 (March) 1938.

A case of acute dermatitis following exposure to garlic is described in a child playing in the fields during the harvest of garlic. Only exposed parts were affected, and the lesions were disseminated, vesicular and pustular. The diagnosis was confirmed by skin tests. Eosinophilia (23 per cent) was observed.

SCHLUTZ, Chicago.

PHAGEDENIC ECTHYMA IN AN INFANT. G. CARDELLE, B. SANTIAGO and A. G. LOPEZ, Arch. de med. inf. **7**:380 (July) 1938.

The authors present a case of phagedenic ecthyma in a boy aged 1 year. There was an ulcer on the hypogastrium, extending to the left lumbar region, and there were other smaller ones on the back and extremities.

Cultures showed the hemolytic streptococcus.

The spread was rapid but without much necrosis, and the general symptoms were pronounced.

Local applications of an antiseptic paste and gentian violet were used in the course of treatment. Blood transfusions were also given. SCHLUTZ, Chicago.

AVITAMINOTIC EDEMA OF INFANCY. CHAVARRÍA, A. PEÑA and W. ROTTER, Rev. méd. latino-am. **23**:1027 (June) 1938.

This condition, hitherto rare, was observed in 43 children, or 1 per cent of those admitted to pediatric hospitals in Costa Rica in less than three years. Most of the children came from poverty-stricken, insanitary homes in the city, and 31 of them were less than 5 years of age. The clinical picture was more or less similar in all instances; the children were apathetic, undernourished and wretched, crying out in pain when moved; some had photophobia; anorexia was extremely common; those who could walk had a swaying or spastic gait; mucous diarrhea was almost universal. There was a variable amount of edema of the feet, hands and face and in some cases generalized anasarca. The mucous membranes of the mouth were red, with pallid streaks resembling atrophy, and at the oral commissures were heaped-up erosions. The tongue was smooth and red; the hair was dry and silky and was coming out in bunches. In the early stages the skin of the hands and feet was smooth and of a reddish or cyanotic hue, which diminished gradually as it progressed upward but lacked completely any sharp line of demarcation. The skin was cold. After the acute phase had passed, the skin in these areas desquamated, became pigmented and at times showed vesicles and bullae. More rarely, there were indolent ulcers and hemorrhagic lesions.

Of the 43 patients studied, 17 died, but these were practically moribund on admission; in most instances the cause of death was intercurrent pneumonia or bronchopneumonia. At autopsy one observed, in addition to the lesions already noted, fluid in the body cavities, atrophic colitis and fatty changes in the liver.

When the condition is favorable, the response to dietary therapy is amazingly rapid; the diet consists chiefly of milk, cereal gruels, cod liver oil and orange juice.

The authors conclude that the condition is a true avitaminosis, corresponding to incipient beriberi and pellagra, with an element of scurvy in some cases. They note that its increase is coincidental with the economic depression. They note the similarity to the condition called erythredema but feel that the response to diet justifies the appellation of avitaminotic edema.

LEIFER, New York. [ARCH. DERMAT. & SYPH.]

HISTOPATHOLOGY OF OSLER'S DISEASE (HEREDITARY HEMORRHAGIC TELANGIECTASIA). A. FINGERLAND and B. JANOUSEK, Arch. f. Dermat. u. Syph. **178**:54, 1938.

Fingerland and Janousek report the case of a woman aged 27 who had suffered from frequent profuse epistaxis from early youth up to the age of 22. Numerous telangiectatic lesions were present on the forearm and soft palate. Ten of the patient's relatives suffered from nosebleed. Microscopic examination revealed papillary telangiectasis. The dilated vessels occasionally showed thrombosis and hyaline degeneration, with hemorrhage into the surrounding tissue. The collagenous and elastic tissue were normal. The walls of the venules were thickened, owing to noninflammatory increase of the muscle cells or adventitial cells. The author concludes that such thickening narrows the lumen, increases the pressure in the capillaries and results in capillary dilatation.

BECKER, Chicago. [ARCH. DERMAT & SYPH.]

ALLERGY IN INFANTS. P. WORINGER, Pediatria polska **18**:149 (March) 1938.

The most interesting observation Woringer has made is that allergy is most frequent in infants in the first year of life. He presents a detailed article on

allergy in infants, discussing different theories, particularly that of inheritance and of sensitization via the placenta during gestation. He states that since the investigations of Portier, Richet and Arthus nothing new has been added to the science of allergy and anaphylaxis. The infant can inherit allergy from either the mother or the father.

KRUPINSKI, Chicago.

PROBLEM OF LIVEDO TELANGIECTATICA CONGENITA GENERALISATA. S. NEUMARK, Acta dermat.-venereol. **19**:316 (May) 1938.

Neumark describes a case of extensive livedo reticularis in an undernourished girl of 3 years. At birth she presented a deep blue discoloration of the entire skin, including the visible mucous membranes. Only after three or four months did normally colored areas begin to appear; these enlarged gradually. At the age of 3 years she presented numerous telangiectatic spots, which were most pronounced on the face and extremities. A spontaneous gradual improvement took place during eight years' observation. The author believes that livedo reticularis is caused by disturbances in the development of the vascular system, consisting of dilatation of the blood vessels, together with proliferation of new vessels in the connective tissue. There is also diminution—almost total absence—of elastic fibers in the outer walls and in the vicinity of the dilated and multiplied vessels of the superficial parts of the cutis.

ASTRACHAN, New York. [ARCH. DERMAT. & SYPH.]

Surgery and Orthopedics

PLASTIC SURGERY IN CHILDREN: THE MEDICAL AND PSYCHOLOGIC ASPECTS OF DEFORMITY. C. L. STRAITH and E. H. DE KLEINE, J. A. M. A. **111**:2364 (Dec. 24) 1938.

The authors review the treatment of some of the common deformities in children which require plastic surgical procedures for their correction and discuss the psychologic effects of such deformities. Harelip, scars from burns and dirty abrasions, deformities of the nose, lop ears and ptosis of the eyelids are examples of conditions which may produce marked changes in personality. These results must be kept in mind as well as the functional derangement in planning prophylactic and therapeutic care. Besides the effort at complete correction, in many cases especial care should be taken to enable patients to compensate for their handicap.

HEERSMA, Kalamazoo, Mich.

MUSCLE DYSTROPHIES AND ATROPHIES OCCURRING IN CHILDHOOD: FROM THE ORTHOPEDIC ASPECT. A. R. HAMILTON, M. J. Australia **2**:887 (Nov. 26) 1938.

The conditions under discussion are divided into two groups: (1) those which are congenital and (2) those which appear after birth.

Group 1.—(*a*) Congenital high shoulder (Sprengler's). This occurs as a result of failure of a muscle mass connecting the skull to the scapula to develop beyond the myoblastic stage, with presence of excessive fibrous tissue in those muscles.

(*b*) Tibial kyphosis. This is due to failure of the calf muscles to grow in length even though fully differentiated.

(*c*) Myodystrophia foetalis deformans. This affects the upper and lower extremities and results in any one of the following: congenital genu recurvatum, clubfoot or clubhand, congenital dislocation of the hip, absence of the patella, limitation of joint movements, flexion deformity of joints. The muscle development here is decidedly abnormal and treatment correspondingly difficult.

(*d*) Congenital torticollis. It is probably due to venous obstruction in the sternocleidomastoid causing some fibrosis.

(*e*) Amyotonia congenita. The treatment advocated is designed to prevent overstretching of the joint capsule and ligaments.

Group 2.—(*a*) Pseudohypertrophic muscular paralysis. It should not be regarded as hopeless, for it may become stationary for a considerable period of time so that every effort should be made to prevent deformities.

(*b*) Anterior poliomyelitis. This calls for splinting in the early stages of the disease.

(*c*) Volkmann's contracture. It is possible to prevent venous congestion by incision in the cubital fossa if the patient is seen early.

TENNEY, Madison, Wis.

SUBPERIOSTEAL RESECTION OF THE ULNA. G. HERZFELD, Tr. Med.-Chir. Soc. Edinburgh, 1938, p. 190; in Edinburgh M. J., October 1938.

A boy now 9½ years old shows the end result of an operation in which a subperiosteal resection was performed for extensive tuberculosis that had involved a long bone since the age of 18 months. Although the metacarpal and the upper two thirds of the ulna were removed, the boy still possesses a very useful forearm. There is slight restriction of movement at the elbow.

NEFF, Kansas City, Mo.

Miscellaneous

GIRLS ON PAROLE—AND AFTER. M. SKODAK, J. Juvenile Research **22**:145 (July-Oct.) 1938.

Girls who had been confined to the Iowa State Training School for Girls and who had then been discharged or paroled were studied as to their ability to make adjustments after such institutionalization. The findings showed that they tended to adjust but that at first one-quarter were successful whereas after a period of months three-quarters accepted the standards of those among whom they found themselves. Whether or not marriage helped toward adjustment depended on the type of man married.

HAMILL, Chicago.

LEAD COLIC. J. COLUMBE, Arch. de méd. d. enf. **42**:103 (Feb.) 1939.

Two brothers, aged 4 and 6, respectively, were seized in the space of twenty-four hours with violent abdominal pain and vomiting but with no objective signs to assist in diagnosis. Belladonna gave no relief; one of the boys was constipated, and suppositories were used without result. The picture gradually assumed that of saturnism, and it was then recalled that two days before the symptoms appeared the children had played with red paint for a few minutes in a closed garage. Albumin was found in the urine of both boys, and one suffered from severe myalgia in addition to the colic. The blood showed no basophilic granulations and only slight anemia. The extreme sensibility of the young organism to lead poisoning is pointed out.

AMESSE, Denver.

STUDY OF THE ACTION OF SULFANILAMIDE. M. PORRO VARELA, Bol. coll. med. Camaguey **1**:19 (Oct.-Dec.) 1938.

The author reviews the literature on the indications for the action and the toxicity of sulfanilamide. This drug does not act directly on the reticuloendothelial system but exerts its beneficial action by bactericidal and bacteriostatic properties, diminishing the virulence of the organisms and inhibiting the production of toxins. It is most effective against the beta type of hemolytic streptococcus.

DWYER, Kansas City, Mo.

CLINICAL AND RADIOLOGIC STUDIES OF LEAD POISONING. R. PEREIRAS and B. S. SANTIAGO, Bol. Soc. cubana de pediat. **10**:611 (Nov.) 1938.

Pereiras and Santiago presented lead poisoning in 9 children ranging in age from 2 to 9 years. The main symptoms were pallor, anorexia, insomnia and abdominal pain. The lead line of the gums was present in most of these patients; basophilic stippling was observed in 3. Lead deposits were always present in the metaphysis.

SCHLUTZ, Chicago.

LEAD POISONING PRODUCED BY IRRADIATED LEAD. S. NOSU and H. FUJII, Acta pædiat. japon. **44**:1203 (Aug.) 1938.

Lead irradiated with ultraviolet rays appears to have greatly increased toxicity, as determined by the percental increase of basophilic stippled erythrocytes in the blood of rabbits poisoned with the metal.

KATO, Chicago.

Society Transactions

CHICAGO PEDIATRIC SOCIETY

JOSEPH K. CALVIN, M.D., *President*

Regular Meeting, April 18, 1939

GEORGE F. MUNNS, M.D., *Secretary*

MODIFICATION OF SMALLPOX VACCINATION OF SUSCEPTIBLE INFANTS BY SPECIFIC CONVALESCENT SERUM. DR. JOSEPH GREENGARD and DR. ALBERT M. WOLF.

This paper will be published in full in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

HABIT FORMATION. DR. BERT I. BEVERLY.

It is generally agreed that all behavior is expressed in terms of habit and that habits formed during infancy are most important. Even though more has been written on this subject than on any other phase of child development, there are still unduly divergent opinions regarding fundamental problems. There is uncertainty as to what habits are most important, when and how they should develop, which are desirable, undesirable or even pathologic at a given age and how children presenting undesirable habits should be managed. A survey of the literature discloses that much of this confusion is due to the fact that those who work with children have been primarily interested in the behavior which influences the narrow phase of development with which they are concerned and have ignored the growing child as a whole, as well as the anatomy and physiology of habit formation.

Habits develop from within and in terms of the growth and development of the child. They are influenced by many factors, such as (1) the age of the patient and his individual developmental characteristics, (2) feelings which represent the instinctive, subcortical and unconscious drives back of behavior, (3) the fact that the child reacts as a whole, (4) the fact that he reacts on the environment rather than the environment on him, (5) the child's growth in maturity and his adjustment of instinctive impulses to meet social demands and (6) the tendency of habits to develop normally if the child has sufficient security, confidence in his parents, confidence in himself and an opportunity to grow without undue interference, i.e., to learn for himself. Too vigorous training leads to emotional suppression, which gives rise to confusion, apprehension and resentment. Pathologic habits which may take on the aspects of a neurosis are the result.

Attempts to force children to give up undesirable habits through restriction, fear or ridicule are contraindicated and harmful. Either one should search for the factor causing the undesirable behavior, or the patient should be placed in the best obtainable environment and left alone.

DISCUSSION

DR. ARTHUR H. PARMELEE: Dr. Beverly's paper is extremely important for pediatricians. We, more than other physicians, have the opportunity to correct some of the difficulties mentioned. Dr. Beverly has brought home the realization that the human organism is a unit and that we, as pediatricians, are responsible for a knowledge of the growth and development of the whole body, physical, mental and emotional, and for observing and properly directing its response to its environment. Although the situations Dr. Beverly has cited may sound extreme, we can help to correct the conditions which lead to them. Every day in our

offices we all have to answer questions concerning habit formation, just as they have been outlined, and we have the opportunity to make an impression on the mother and the child which will tend to avoid the disturbances which have been described. Most of us have a fairly good knowledge of physical development. We have a beginning knowledge of normal mental growth and development, but up to the present time apparently most of us, according to my own experience and my conversation with other pediatricians, have completely ignored emotional development. We shall not make any great progress until we are willing to take into account emotional development in its relation to physical development.

One of the most difficult phases of this whole problem is the question of its origin. We can talk to parents, but we cannot change them, and the emotional habits taught to the child have been already so fixed by the parents, by their parents before them and so on that it seems impossible to learn the entire background. The environment in which the parents have been reared leads them to train their children in the same puritanic manner in which they themselves were brought up.

DR. MAURICE L. BLATT: Does Dr. Beverly think that there has been any tendency toward improvement in the physical training of children during the past few years?

DR. BERT I. BEVERLY: Dr. Parmelee made a good point in emphasizing that the more extreme and unusual conditions described are commonly encountered daily in milder forms. In reply to Dr. Blatt's question, improvements are slow and proportional to the understanding of normal growth and development of children.

Book Reviews

Services des enfants assistés et de la protection des enfants du premier age du département de la Seine (Premiére partie, statistique; deuxième partie, rapports annuels). By Dr. Louis Mourier. No price given (government publication). Pp. 347, with 18 tables. Paris: Administration générale de l'assistance publique à Paris, 1938.

This publication consists of the first and second parts of the report for 1937 of the division concerned with administration of public aid in Paris which has to do with supervision of infant and child welfare for the Department of the Seine. The first part comprises the statistical report and the second part the detailed annual report.

Services des enfants assistés et de la protection des enfants du premier age du départment de la Seine (troisième partie, compte financier). Dr. Louis Mourier. No price given (government publication). Pp. 68, with 31 tables. Paris: Administration générale de l'assistance publique à Paris, 1938.

This is the financial report for 1937 of the administration of public funds devoted to infant and child welfare in the Department of the Seine.

Services des enfants assistés du départment de la Seine, 1936. By Dr. Louis Mourier. No price given (government publication). Pp. 68, with 31 tables. Paris: Administration générale de l'assistance publique à Paris, 1937.

This is the financial report for 1936 of the administration of public funds devoted to infant and child welfare in the Department of the Seine.

Studien über Vererbung und Entstehung geistiger Störungen. VI Zur Klinik, Vererbung, Entstehung und Rassenhygiene der angeborenen cerebralen Kinderlähmung (Littleschen Krankheit). Zwillingsbiologische Untersuchungen bei angeborener spastischer Hemi-, Para- und Diplegie (neurologische Zwillingsstudien III. Mitteilung). By Dr. Med. Karl Thums. Edited by Ernst Rüdin. Paper, price, 29.40 marks. Pp. 266, with 28 illustrations. Berlin: Julius Springer, 1939.

This is no. 66 of the excellent series of monographs on neurologic and psychiatric subjects edited by Bumke, Foerster, Rüdin and Spatz. It is a veritable cyclopedia on the subject of birth palsies. It emphasizes the importance of the subject to a country the government of which is conscious of its racial-political responsibilities and wishes to make practical use of the scientific study of heredity. In the excellent historical review it is indicated that while Oppenheim treated cerebral infantile palsy and Little's disease in separate chapters, Freud had pointed out the lack of difference between the two diseases. Certain conditions formerly included in this group are now eliminated, namely, familial spastic spinal paralysis, familial diffuse sclerosis, the Pelizaeus-Merzbacher disease, Schilder's disease, amaurotic family idiocy and tuberous sclerosis. The greater part of the book is devoted to the problem of the relative importance of genetic conditions and birth trauma. Dr. Thums secured complete data concerning 90 pairs of twins, in each of which at least a single twin had some form of birth palsy. The careful analysis of this material shows clearly that heredity is unimportant and that injury at birth is the main factor.

Scarlet Fever. By George F. Dick, M.D., and Gladys Henry Dick, M.D. Price, cloth, $2. Pp. 149, with 8 color plates. Chicago: The Year Book Publishers, Inc., 1938.

This book is a valuable record of the authors' work on scarlet fever. The opening chapter contains a short history of scarlet fever. In the second chapter, entitled "Etiology," there is considerable discussion of antibacterial serums and of the preparation of scarlet fever antitoxin. Chapters 3, 4, 5, 6 and 7 briefly set forth important information on pathologic anatomy, symptoms, varieties of scarlet fever, complications and diagnosis and prognosis. Chapter 8, which deals with treatment, emphasizes the value of scarlet fever antitoxin. It contains four fever charts, which may be misleading to one not familiar with the disease.

Other chapters are concerned with the preparation of scarlet fever antitoxin, the skin test for susceptibility to scarlet fever, prophylaxis, the specificity of hemolytic streptococci, allergy, antibacterial immunity and local immunity and oral immunization, in this order.

Descriptions of the successful accomplishments of the authors are naturally interwoven throughout the treatise. There is left no suspicion of the possibility of error in respect to conclusions.

Eight excellent color plates illustrate reactions of the Dick test and other features associated with scarlet fever. A bibliography contains a splendid list of references. The book should appeal to those especially engaged in the study of scarlet fever.

Sex and Internal Secretions: A Survey of Recent Research. Edited by Edgar Allen, C. H. Danford and E. A. Doisy. Second edition. Price, $12. Pp. 1,346, with 452 illustrations, 3 color plates and 42 tables. Baltimore: Williams & Wilkins Company, 1939.

The present edition of this well known work will be favorably received by every investigator in the field of endocrinology. Since the first appearance of the book, in 1932, so much has been learned about the sex hormones and the interrelationships of the endocrine glands that a second edition has become necessary. Twenty-seven authors, all active investigators in the subjects they discuss, have contributed to this exhaustive survey. In addition to the material contained in the first edition, a few new chapters deserve special mention. Progress made in the chemistry of the androgenic and estrogenic hormones and of the hormones of the corpus luteum has been reviewed in special sections by F. C. Koch, E. A. Doisy, W. M. Allen and others. The cytology of the anterior lobe of the pituitary gland in relation to the reproductive hormone has been discussed by A. E. Sevringhaus. Physicians will be particularly interested in the chapters on the lactogenic hormone, by O. Riddle and R. W. Bates, on the relation of the thymus and the pineal gland to genital function, by W. O. Nelson; on the relation of the vitamins to the sex glands, by K. E. Mason, and on the sexual functions in human beings, by J. P. Pratt. They will note, however, the lack of a complete discussion of the relation of the adrenal glands to the gonads and their functions.

The Physiology and Pharmacology of the Pituitary Body. Volume II. By H. B. Van Dyke, M.D. Price, $4.50. Pp. 402, with 28 illustrations and 10 tables. Chicago: University of Chicago Press, 1939.

In 1936 the first volume of this work reviewed the immense accumulation of literature on the functions of the pituitary gland. The bibliography of some three thousand references has become indispensable to every investigator in this field. Since then the number of publications on the functions and interrelationships of the hypophysis has not decreased. Dr. Van Dyke estimates that about seven hundred and fifty articles appear each year in this field, an amount of literature too large for the individual investigator to examine. Volume II, a critical review of the publications that have appeared between 1935 and 1939, becomes a necessary

supplement to the first volume. A bibliography of over fourteen hundred titles follows a survey of recent progress in the investigation of the pituitary gland. The chapters on the relation of the pars glandularis to lactation and metabolism are particularly interesting to the pediatrician. The recent investigations on the physiology of the pars neuralis are ably surveyed and discussed.

The Clinical and Experimental Use of Sulfanilamide, Sulfapyridine and Allied Compounds. By Perrin H. Long, M.D., and Eleanor A. Bliss, Sc.D. Price, $3.50. Pp. 319, with 6 charts. New York: The Macmillan Company, 1939.

The seven chapters deal with the historical aspects of sulfanilamide therapy, the chemotherapy of experimental bacterial infections, the experimental toxicity and the comparative pharmacology of sulfanilamide and allied compounds, the mode of action of sulfanilamide and its derivatives, the clinical use of sulfanilamide, the clinical use of sulfapyridine, of sulfanilyl sulfanilamide and of benzylsulfanilamide, the clinical use of prontosil and neoprontosil and the clinical toxic manifestations of sulfanilamide and its derivatives. The book will be found most useful for its chapter on historical aspects and its many references. The authors were perhaps too dogmatic in their own views and too caustically critical of other workers in this field who have expressed opposing views. As usual with a rapidly advancing subject, the textbook which attempts to cover it is already almost out of date when published.

The Newer Knowledge of Nutrition. By E. V. McCollum, Elsa Orent-Keiles and Harry G. Day. Fifth edition. Price, $4.50. Pp. 701, with 18 photographs. New York: The MacMillan Company, 1939.

This edition of the book (the fourth was published in 1929) has been entirely rewritten. However, the original plan and scope of the work have been retained. Roughly, the plan is to trace the science of nutrition through its historical background and to discuss the various dietary requirements of mankind. These are carbohydrates, fats, proteins, minerals and vitamins. The final chapters deal with the dietary properties of foodstuffs, with appetite and with dietary habits. An enormous task has been satisfactorily completed. Of especial interest are the chapters on the vitamins, which carry the references in the literature to the present. Every chapter carries a complete bibliography. This book should be read by every member of the medical profession. It is excellently printed and would be an invaluable addition to any library.

Syphilis and Its Accomplices in Mischief: Society, the State and the Physician. By Dr. George M. Katsainos. Price, $5. Pp. 676, with no illustrations. Athens, Greece: Privately printed, 1939.

This book consists of the main portion (554 pages) and an appendix (162 pages), a treatise on eugenics entitled "Marriage and Syphilis."

In the epilogue Dr. Katsainos remarks, "What was wrong with it to be so unanimously refused by every publisher, medical or lay, to whom it was transmitted, I do not know, and I was never permitted, as I have already told, to know." His purpose in writing the book was "to clear syphilis of its asyphilon [stigma]."

The work is verbose, and the medical material is incoherently mixed with the author's private opinions, salted down with sprinklings of Greek mythology.

Encefalitis postneumonica en el nino. By Jose Bonaba and Carlos M. Barberousse. Paper, price not given. Pp. 101, with 9 illustrations. Montevideo, Uruguay: Rosgal de Hilario Rosillo, 1939.

This is no. 5 of the series of monographs from the pediatric clinic of Dr. Luis Morquio. The authors have collected 28 cases of postpneumonic encephalitis from the literature and have discussed symptoms, diagnosis, pathology and treat-

ment. Excellent plates show the pathologic features, and there is a full bibliography. The authors consider this complication to be a distinct clinical entity and worthy of study. The discussions are excellent.

The Throat Distemper of 1735-1740. By Ernest Caulfield, M.D. No price given. Pp. 113, with 43 illustrations. New Haven, Conn.: The Yale Journal of Biology and Medicine, 1939.

This book represents the best type of historical medical research. It was carefully done, and Dr. Caulfield spared no pains in following every clew available. His clear demonstration that this throat distemper was not only scarlet fever but diphtheria, and his ability to distinguish very largely between the different epidemics alone would make this a valuable contribution. Aside from presenting the medical material, the book gives one valuable insight into the times from a unique angle.

Pitannya akusherstva i ginekologii. A symposium edited by A. M. Gasparyan and Prof. P. X. Chajinsky. No price given. Pp. 140. Kiev, U. S. S. R.: 1938.

This book on procedures in obstetrics and gynecology was written in Ukranian and published under the auspices of the Medical Institute of Charkov. It is a symposium of lectures given by various members of the Department of Obstetrics and Gynecology of the institute, under the direction of Prof. P. X. Chajinski. The material is confined entirely to technical and operative procedures and presents no aspects of any interest from the pediatric standpoint.

Raquitismo. By Juan P. Garrahan. Paper, price not given. Pp. 167, with 50 illustrations. Buenos Aires, Argentina: El Ateneo, 1939.

This excellent monograph on rickets contains the usual studies of age, symptoms, clinical signs and prognosis, with observations on the chemistry of calcium and phosphorus. It includes a chapter on rickets in premature infants and a chapter on the action of antirachitic remedies. The illustrations and diagrams are well chosen, and the bibliography is complete.

Ensayo de investigacion de la mortalidad infantil en san salvador y algunas sugerencias para combatirla. By Andres G. Funes and Ranulfo Castro. Paper, price not given. Pp. 101, with 12 illustrations. San Salvador, El Salvador: Poencia Oficial De El Salvadore, 1939.

This report of the Committee of the Medical Congress of San Salvador contains an excellent discussion of the various causes of infant mortality. The numerous charts and diagrams should be studied in detail.

Directory of Pediatric Societies*

INTERNATIONAL

International Association of Preventive Pediatrics

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Prof. Luigi Spolverini, Policlinico Lungo Tevere Melini 24, Rome, Italy.
Secretary: Professor Vitetti, Rome, Italy.
Place: Boston. Time: Sept. 3-5, 1940.
American Committee:
Chairman: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
General Secretary: Dr. Kenneth D. Blackfan, 300 Longwood Ave., Boston.
Assistant Secretary-Treasurer: Dr. Charles F. McKhann, 300 Longwood Ave., Boston.
Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St. W., Montreal.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

FOREIGN

Argentine Pediatric Society of Buenos Aires

President: Dr. Martin Ramón Arana, 1809 Rodriguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Larguia, Cerrito 1179, Buenos Aires.

British Paediatric Association

President: Dr. Hector C. Cameron, 23 Devonshire Pl., Upper Wimpole St., London, W. 1.
Secretary: Dr. Arthur G. Maitland Jones, 31A Weymouth St., London, W. 1.

Danish Pediatric Society

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. E. Gjørup, Dronning Louises Børnehospital, Copenhagen.

Paediatrický Spolok na Slovensku

President: Dr. A. J. C. Chura, Lazaretská 11, Bratislava.
Secretary: Dr. P. Rados, Lazaretská 6, Bratislava.
Place: Pediatric Clinic, University Bratislava. Time: Six times a year.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. E. A. Cockayne, 98 Harley St., London, W. 1, England.
Secretary: Dr. R. Lightwood, 86 Brook St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

Palestine Jewish Medical Association, Section of Physicians of Children's Diseases

President: Prof. S. Rosenbaum, 26 Bialikstr., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

SOCIEDAD CUBANA DE PEDIATRÍA

President: Dr. Clemente Inclan Costa, Manrique 48, Habana.
Secretary: Dr. Serafin Falcon Lopez, Calle B No. 356, Vedado, Habana.
Place: Cátedra de Clinica Infantil, Hospital Mercedes, Habana. Time: Last Wednesday of every month.

SOCIÉTÉ DE PÉDIATRIE DE PARIS

President: Dr. B. Weill-Hallé, 49 Avenue Raymond Poincaré, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue du Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Malades, 49 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON PEDIATRICS

Chairman: Dr. Albert D. Kaiser, 16 N. Goodman St., Rochester, N. Y.
Secretary: Dr. Hugh L. Dwyer, 315 Alameda Rd., Kansas City, Mo.
Place: New York. Time: June 10-14, 1940.

AMERICAN ACADEMY OF PEDIATRICS

President: Dr. H. F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Place: Netherland Plaza Hotel, Cincinnati. Time: Nov. 16-18, 1939.
Region I. Place: Mayflower Hotel, Washington, D. C. Time: April 4-6, 1940.

AMERICAN HOSPITAL ASSOCIATION, CHILDREN'S HOSPITAL SECTION

Chairman: Miss Mabel Binner, Children's Memorial Hospital, Chicago.
Secretary: Winifred Culbertson, Children's Convalescent Hospital, Cincinnati.

AMERICAN PEDIATRIC SOCIETY

President: Dr. Herbert B. Wilcox, 39 E. 75th St., New York.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. R. R. MacGregor, 142 Wellington St., Kingston, Ontario.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, Hospital for Sick Children, Toronto.

SOCIETY FOR PEDIATRIC RESEARCH

President: Dr. Daniel C. Darrow, 330 Cedar St., New Haven, Conn.
Secretary: Dr.Mitchell I. Rubin, 1740 Bainbridge St., Philadelphia.

SECTIONAL

INTERMOUNTAIN PEDIATRIC SOCIETY

President: Dr. Eugene Smith, 385–24th St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. R. Cannon Eley, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. James Marvin Baty, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. Frederick Fischer, 407 Riverside Ave., Spokane, Wash.
Secretary: Dr. C. L. Lyons, Paulsen Medical-Dental Bldg., Spokane, Wash.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. John Schoonover, Republic Bldg., Denver.
Secretary: Dr. F. Craig Johnson, 1850 Gilpin St., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 7:30 p. m.

SOUTHERN MEDICAL ASSOCIATION, SECTION OF PEDIATRICS

Chairman: Dr. Hughes Kennedy Jr., Highland Plaza Apts., Birmingham, Ala.
Secretary: Dr. Warren W. Quillian, 227 Aragon Ave., Coral Gables, Fla.
Place: Memphis, Tenn. Time: Nov. 21-24, 1939.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. Stewart H. Welch, 1117 S. 20th St., Birmingham.
Secretary-Treasurer: Dr. William R. Britton, 4 Catoma St., Montgomery.

ARKANSAS STATE PEDIATRIC ASSOCIATION

Chairman: Dr. G. D. Murphy, 112 Peach St., El Dorado.
Secretary: Dr. Madeline M. Melson, 909 Main St., Little Rock.

CALIFORNIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. Harold K. Faber, 2341 Clay St., San Francisco.
Secretary: Dr. Hartzel H. Ray, 23–2d Ave., San Mateo.

FLORIDA STATE PEDIATRIC SOCIETY

President: Dr. Gilbert S. Osincup, 300 E. Colonial Dr., Orlando.
Secretary: Dr. Warren W. Quillian, 227 Aragon Ave., Coral Gables.
Place: Concurrent with state association meeting at time of convention.

GEORGIA PEDIATRIC SOCIETY

President: Dr. L. H. Muse, 384 Peachtree St. N. E., Atlanta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta
Scientific Meeting: Place: Atlanta. Time: December 1939. Business Meeting: Place: Savannah. Time: April 1940.

HEZEKIAH BEARDSLEY PEDIATRIC CLUB OF CONNECTICUT

President: Dr. C. V. Calvin, 144 Golden Hill St., Bridgeport.
Secretary: Dr. E. T. Wakeman, 129 Whitney Ave., New Haven.
Time: Three meetings a year.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. O. N. Torian, 23 E. Ohio St., Indianapolis.
Secretary-Treasurer: Dr. Mathew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

IOWA PEDIATRIC SOCIETY

President: Dr. Morgan J. Foster, 837 Higley Bldg., Cedar Rapids.
Secretary-Treasurer: Dr. Arnold M. Smythe, 406–6th Ave., Des Moines.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. Phillip C. De Verges, Audubon Bldg., New Orleans.
Secretary-Treasurer: Dr. W. C. Rivenbark, 220 Physicians and Surgeons Bldg., New Orleans.

MEDICAL SOCIETY OF STATE OF NEW YORK, SECTION ON PEDIATRICS

Chairman: Dr. Paul W. Beaven, 26 S. Goodman St., Rochester.
Secretary: Dr. Leslie O. Ashton, 842 Park Ave., New York.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, PEDIATRIC SECTION

Chairman: Dr. John M. Higgins, 600 S. Wilbur Ave., Sayre.
Secretary: Dr. John D. Sturgeon Jr., 22 N. Gallatin Ave., Uniontown.

MICHIGAN STATE MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Allan L. Richardson, 3001 W. Grand Blvd., Detroit.
Secretary: Dr. Ward L. Chadwick, 524 Medical Arts Bldg., Grand Rapids.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Secretary-Treasurer: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Place: To be designated by society. Time: Yearly.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. Herman M. Jahr, 1120 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. Elmer W. Bantin, 440 Aquila Court Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Marion Y. Keith, 369 N. Elm St., Greensboro.
Secretary: Dr. G. W. Kutscher Jr., 176 Woodfin St., Asheville.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. A. L. Salomon, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. Ben H. Nicholson, 301 W. 12th St., Oklahoma City.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. D. Lesesne Smith Jr., 187 Oakland Ave., Spartanburg.
Secretary-Treasurer: Dr. William Weston Jr., 1428 Lady St., Columbia.

TENNESSEE STATE PEDIATRIC SOCIETY

President: Dr. William E. Van Order, 546 McCallie Ave., Chattanooga.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.

TEXAS PEDIATRIC SOCIETY

President: T. A. Tumbleson, 2100 North St., Beaumont.
Secretary-Treasurer: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Place: Fort Worth. Time: Oct. 14, 1939.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. W. Ambrose McGee, 616 W. Grace St., Richmond.
Secretary: Dr. John M. Bishop, Medical Arts Bldg., Roanoke.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. J. L. Blanton, 207 Fairmont Ave., Fairmont.
Secretary: Dr. Theresa O. Snaith, 450 Center Ave., Weston.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. N. C. Wetzel, 2103 Adelbert Rd., Cleveland.
Secretary: Dr. Fred Rittenger, 10515 Carnegie Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. T. B. Verner, 170 St. George St., Toronto, Canada.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto, Canada.

BRONX PEDIATRIC SOCIETY

President: Dr. Samuel T. Levethan, 254 E. 184th St., Grand Concourse, New York.
Secretary: Dr. David Greene, 910 Grand Concourse, New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

BROOKLYN ACADEMY OF PEDIATRICS

President: Dr. Benjamin Kramer, 6 Pierrepont St., Brooklyn.
Secretary: Dr. John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank van der Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Gerard N. Krost, 2376 E. 71st St., Chicago.
Secretary: Dr. George F. Munns, 723 Elm St., Winnetka, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

DALLAS PEDIATRIC SOCIETY

President: Dr. Harold Nesbit, 1719 Pacific Ave., Dallas, Texas.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmont Ave., Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

DETROIT PEDIATRIC SOCIETY

President: Dr. William O'Donnell, 1553 Woodward Ave., Detroit.
Secretary: Dr. Robert Mason, 5140-2d Blvd., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

FULTON COUNTY MEDICAL SOCIETY, PEDIATRIC SECTION (ATLANTA, GA.)

Chairman: Dr. L. H. Goldsmith, 384 Peachtree St. N. E., Atlanta.
Secretary: Dr. James P. Hanner, 384 Peachtree St. N. E., Atlanta.
Place: Academy of Medicine, 38 Prescott St. N. E. Time: Second Thursday of each month from October to April, 8 p. m.

HOUSTON PEDIATRIC SOCIETY

President: Dr. James H. Park Jr., 3717 Main St., Houston, Texas.
Secretary-Treasurer: Dr. Thomas J. Donovan, 2418 Travis St., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

KANSAS CITY (MISSOURI) PEDIATRIC SOCIETY

President: Dr. Urban Busiek, 200 E. Pershing St., Springfield, Mo.
Secretary: Dr. Fred Speer, 2700 Parallel Ave., Kansas City, Kan.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. H. R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Paul M. Hamilton, 248 E. Main St., Alhambra, Calif.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd.
Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Benjamin Stoloff, 1149 Eastern Parkway, Brooklyn.
Secretary: Dr. Harry Apfel, 988 Park Pl., Brooklyn, N. Y.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m., second Monday of each month, October to March, inclusive.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. James Dobbins, 42-04 Ditmars Blvd., Long Island City, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144–38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Medical Society of the District of Columbia, Section on Pediatrics

President: Dr. Harry H. Donnally, 1612 I St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. Harry A. Spigel, 2647 Connecticut Ave. N. W., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time: 8 p. m., fourth Thursday of October, January, February, March and April.

Memphis Pediatric Society

President: Dr. Barton Etter, 376 S. Bellevue St., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: John Gaston Hospital. Time: Quarterly.

Milwaukee Pediatric Society

President: Dr. Helen Jane Zillmer, 781 N. Jefferson St., Milwaukee.
Secretary-Treasurer: Dr. Samuel E. Kohn, 425 E. Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Philip M. Stimson, 25 Claremont Ave., New York.
Secretary: Dr. Lucy Porter Sutton, 168 E. 74th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northwestern Pediatric Society

President: Dr. Robert Rosenthal, 437 Lowry Medical Arts Bldg., St. Paul.
Secretary-Treasurer: Dr. R. E. Nutting, 205 W. 2d St., Duluth, Minn.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Oklahoma City Pediatric Society

President: Dr. A. L. Salomon, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 1200 N. Walker St., Oklahoma City.
Time: Every month, except June, July and August.

Philadelphia Pediatric Society

President: Dr. Samuel Goldberg, 4546 N. Broad St., Philadelphia.
Secretary: Dr. Aims C. McGuinness, Children's Hospital, 1740 Bainbridge St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to April, inclusive.

Pittsburgh Pediatric Society

President: Dr. James LeRoy Foster, Highland Bldg., Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200–5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate month from October to June, inclusive.

Richmond Pediatric Society

President: Dr. Emily Gardner, 1100 W. Franklin St., Richmond, Va.
Secretary-Treasurer: Dr. T. Stanley Meade, 913 Floyd Ave., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: 8 p. m., first Thursday of each month, except July, August and September.

Rochester Pediatric Society

President: Dr. David Wolin, 16 N. Goodman St., Rochester, N. Y.
Secretary: Dr. H. C. Soule, 16 N. Goodman St., Rochester, N. Y.
Place: Rochester Academy of Medicine or arrangement by program committee. Time: Second Friday of each month.

St. Louis Pediatric Society

President: Dr. Ralph L. Cook, 508 N. Grand Blvd., St. Louis.
Secretary-Treasurer: Dr. Peter G. Danis, 634 N. Grand Blvd., St. Louis.
Place: St. Louis Medical Society Bldg. Time: Third Friday of each month from September to June.

Seattle Pediatric Society

President: Dr. Jay I. Durand, 1305–4th Ave., Seattle.
Secretary: Dr. Frederick B. Joy, 1215–4th Ave., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

Southwestern Pediatric Society

President: Dr. E. Earl Moody, 829 S. Alvarado Ave., Los Angeles.
Secretary: Dr. Norman Nixon, 1136 W. 6th St., Los Angeles.
Place: Jonathan Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Clement Smith, 1101 Beacon St., Brookline, Mass.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.

Westchester County Medical Society, Pediatric Section (New York)

President: Dr. Norman Survis, 650 Main St., New Rochelle.
Secretary-Treasurer: Dr. Elvira Ostlund, 131 Purchase St., Rye.
Place: Grasslands Hospital, Valhalla, N. Y. Time: Third Thursday in October, December, February and April.